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NEWS 7 Apr 22 BIOSIS Gene Names now available in TOXCENTER
NEWS 8 Apr 22 Federal Research in Progress (FEDRIP) now available
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NEWS 23 Sep 03 JAPIO has been reloaded and enhanced
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NEWS 26 Sep 16 CA Section Thesaurus available in CAPLUS and CA
NEWS 27 Oct 01 CASREACT Enriched with Reactions from 1907 to 1985
NEWS 28 Oct 21 EVENTLINE has been reloaded
NEWS 29 Oct 24 BEILSTEIN adds new search fields
NEWS 30 Oct 24 Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 31 Oct 25 MEDLINE SDI run of October 8, 2002

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=> s TNF receptor associated with death protein? or Tnf receptor associated death protein
L1 1 TNF RECEPTOR ASSOCIATED WITH DEATH PROTEIN? OR TNF RECEPTOR
ASSOCIATED DEATH PROTEIN

=> d bib abs

L1 ANSWER 1 OF 1 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1998:458095 BIOSIS
DN PREV199800458095
TI Adenovirus E3-14.7K protein does not prevent apoptosis by ***TNF*** - ***receptor*** ***associated*** ***death*** ***proteins*** or caspases.
AU Schneider-Brachert, W.; Schlaak, C.; Davarnia, P.; Marget, M.; Kroenke, M.
CS Inst. Immunol., Univ. Kiel, Michaelisstr. 5, D-24105 Kiel Germany
SO Journal of Interferon and Cytokine Research, (May, 1998) Vol. 18, No. 5, pp. A76.
Meeting Info.: 7th International Conference on Tumor Necrosis Factor and Related Molecules Scientific Advances and Medical Applications Hyannis, Massachusetts, USA May 17-21, 1998
ISSN: 1079-9907.
DT Conference
LA English

=> s TRADE alpha or TRADE beta
L2 3 TRADE ALPHA OR TRADE BETA

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3 3 DUP REM L2 (0 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 3 ANSWERS - CONTINUE? Y/(N):y

L3 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2002 ACS
AN 2001:598038 CAPLUS
DN 135:175423
TI TRADE molecules and uses related thereto
IN Wood, Clive; Chaudhary, Divya; Long, Andrew
PA Genetics Institute, Inc., USA
SO PCT Int. Appl., 173 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001058954	A2	20010816	WO 2001-US4238	20010209
WO 2001058954	A3	20020321		
US 2002068696	A1	20020606	US 2001-780532	20010209
PRAI US 2000-181922P	P	20000211		
US 2000-182148P	P	20000214		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AB The present invention relates, at least in part, to methods of modulating proliferation and apoptotic state of cells using agents that modulate the expression and/or activity of TRADE family polypeptides. In addn., the invention provides two novel members of the TRADE family of mols.

L3 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:408685 BIOSIS
DN PREV200000408685
TI TRADE: A novel TNF-receptor family member.
AU Long, Andrew J. (1); Bourque, Karen (1); Chaudhary, Divya (1); Haga, Hisanori; Tada, Hideaki; Burgess, Paul (1); Whitters, Matthew (1); Tan, Xiang Yan (1); O'Hara, Denise (1); Fitz, Lori (1); Beier, David; McCoy, John (1); Collins, Mary (1); Shibayama, Shiro; Wood, Clive R. (1)
CS (1) Genetics Institute, Inc., Wyeth Ayerst Research, Cambridge, MA, 02140 USA
SO Scandinavian Journal of Immunology, (June, 2000) Vol. 51, No. Supplement 1, pp. 64. print.
Meeting Info.: 8th International TNF Congress, Conference on Tumor Necrosis Factor and Related Molecules Scientific Advances and Medical Applications Trondheim, Norway May 14-18, 2000
ISSN: 0300-9475.
DT Conference
LA English
SL English

L3 ANSWER 3 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1993:206467 BIOSIS

DN PREV199395107692
TI Kinetic studies during enzyme hydrolysis of potato and cassava starches.
AU Gorinstein, Shela
CS Dep. Pharmaceutical Chem., Sch. Pharmacy, Hebrew Univ. Jerusalem, Fac. Med., P.O. Box 12065, Jerusalem 91120 Israel
SO Starch, (1993) Vol. 45, No. 3, pp. 91-95.
ISSN: 0038-9056.
DT Article
LA English
SL English; German
AB The hydrolysis of raw potato and cassava starches by bacterial alpha-amylase depends on the time of action, temperature and on the specific starch involved. The molecular weight of the ***trade*** ***alpha*** -amylase (Termamyl 60L), determined by SDS-PAGE, was found to be 55-65 kDa. The properties of alpha-amylase such as kinetic parameters, inhibition, stability, and thermostability were studied. The constants K-m and maximum reaction rate V-max for alpha-amylase were fitted to Michaelis-Menten models with these two starches. Differences in response of potato and cassava starches to hydrolysis by Termamyl 60L can explain differences found in K-m and V-max values and inhibition properties.

=> s TNF receptor famil?
L4 599 TNF RECEPTOR FAMIL?

=> s l4 and trade
L5 2 L4 AND TRADE

=> dup rem l5
PROCESSING COMPLETED FOR L5
L6 2 DUP REM L5 (0 DUPLICATES REMOVED)

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(FILE 'HOME' ENTERED AT 14:56:09 ON 06 NOV 2002)

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 14:56:17 ON 06 NOV 2002
L1 1 S TNF RECEPTOR ASSOCIATED WITH DEATH PROTEIN? OR TNF RECEPTOR A
L2 3 S TRADE ALPHA OR TRADE BETA
L3 3 DUP REM L2 (0 DUPLICATES REMOVED)
L4 599 S TNF RECEPTOR FAMIL?
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L7 0 L6 NOT L3

=> d bib abs l6 1-
YOU HAVE REQUESTED DATA FROM 2 ANSWERS - CONTINUE? Y/(N):y

L6 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2002 ACS
AN 2001:598038 CAPLUS
DN 135:175423
TI ***TRADE*** molecules and uses related thereto
IN Wood, Clive; Chaudhary, Divya; Long, Andrew
PA Genetics Institute, Inc., USA
SO PCT Int. Appl., 173 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001058954	A2	20010816	WO 2001-US4238	20010209
WO 2001058954	A3	20020321		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002068696	A1	20020606	US 2001-780532	20010209
PRAI US 2000-181922P	P	20000211		
US 2000-182148P	P	20000214		

AB The present invention relates, at least in part, to methods of modulating proliferation and apoptotic state of cells using agents that modulate the expression and/or activity of ***TRADE*** family polypeptides. In addn., the invention provides two novel members of the ***TRADE*** family of mols.

L6 ANSWER 2 OF 2 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:408685 BIOSIS
DN PREV200000408685
TI ***TRADE*** : A novel ***TNF*** - ***receptor*** ***family*** member.
AU Long, Andrew J. (1); Bourque, Karen (1); Chaudhary, Divya (1); Haga, Hisanori; Tada, Hideaki; Burgess, Paul (1); Whitters, Matthew (1); Tan, Xiang Yan (1); O'Hara, Denise (1); Fitz, Lori (1); Beier, David; McCoy, John (1); Collins, Mary (1); Shibayama, Shiro; Wood, Clive R. (1)
CS (1) Genetics Institute, Inc., Wyeth Ayerst Research, Cambridge, MA, 02140 USA
SO Scandinavian Journal of Immunology, (June, 2000) Vol. 51, No. Supplement 1, pp. 64. print.
Meeting Info.: 8th International TNF Congress, Conference on Tumor Necrosis Factor and Related Molecules Scientific Advances and Medical Applications Trondheim, Norway May 14-18, 2000
ISSN: 0300-9475.
DT Conference
LA English
SL English

=> s OAF065
L8 2 OAF065

=> dup rem l8
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L9 2 DUP REM L8 (0 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 2 ANSWERS - CONTINUE? Y/(N):y

L9 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2002 ACS
AN 2001:598038 CAPLUS
DN 135:175423
TI TRADE molecules and uses related thereto
IN Wood, Clive; Chaudhary, Divya; Long, Andrew
PA Genetics Institute, Inc., USA
SO PCT Int. Appl., 173 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001058954	A2	20010816	WO 2001-US4238	20010209
WO 2001058954	A3	20020321		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002068696	A1	20020606	US 2001-780532	20010209
PRAI US 2000-181922P	P	20000211		
US 2000-182148P	P	20000214		

AB The present invention relates, at least in part, to methods of modulating proliferation and apoptotic state of cells using agents that modulate the expression and/or activity of TRADE family polypeptides. In addn., the invention provides two novel members of the TRADE family of mols.

L9 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS
AN 1998:608707 CAPLUS
DN 129:215729
TI Cloning of cDNA for novel human proteins belong to tumor necrosis factor receptor superfamily
IN Tada, Hideaki; Konishi, Mikio; Fukushima, Daikichi
PA Ono Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9838304	A1	19980903	WO 1998-JP799	19980226

W: JP, KR, US
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

EP 990703	A1	20000405	EP 1998-905674	19980226

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI

PRAI JP 1997-43143	19970227	
WO 1998-JP799	19980226	

AB The cDNA for proteins ***OAF065*** .alpha. and ***OAF065*** .beta. are isolated from human stroma cell line HAS303. ***OAF065*** .alpha. consists of 416 and ***OAF065*** .beta. of 423 amino acids, with identical N-terminal 1-415 residues. The C-terminal Glu-Ala of ***OAF065*** .alpha. is substituted with 8 amino acid residues in ***OAF065*** .beta.. Both protein contains a Cys-rich domain, commonly seen in the extracellular domain of the TNF receptor superfamily. Claimed are methods of recombinant prepn. of the proteins, (monoclonal) antibody to the proteins, oligonucleotide hybridizing to the cDNA, and therapeutics

contg. the protein and/or the antibodies.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s TNF (3a) receptor?
L10 12584 TNF (3A) RECEPTOR?

=> s l10 and review
L11 973 L10 AND REVIEW

=> d bib abs 1-10

L11 ANSWER 1 OF 973 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:531974 BIOSIS
DN PREV200200531974
TI Signaling from cytokine receptors that affect Th1 responses.
AU Hanlon, Allison M.; Jang, Sihyug; Salgame, Padmini (1)
CS (1) Department of Microbiology and Immunology, Temple University School of Medicine, 3400 N. Broad Street, Philadelphia, PA, 19140: salgame@temple.edu USA
SO Frontiers in Bioscience, (May 1, 2002) Vol. 7, No. Cited May 17, 2002, pp. d1247-d1254. http://www.bioscience.org/. online.
ISSN: 1093-4715.
DT General Review
LA English
AB Receptors of the various cytokines although structurally diverse, can yet be grouped into four major families of receptor proteins. Most cytokines that function in the immune system bind to either the Class I or Class II receptor families. Two other important receptor families are the immunoglobulin superfamily ***receptor*** and the ***TNF*** ***receptor*** family. Members of these receptor families also have critical roles in the immune system. A common feature of all these receptor families is that they do not exhibit any intrinsic tyrosine kinase activity. Receptor signaling is initiated through recruitment of kinases and through recruitment of cytosolic proteins to the receptor. In this ***review*** we will examine receptor signaling pathways initiated from five receptors that are all involved in either initiating T helper-1 (Th1) responses, or in downregulating Th1 responses. The following receptors: Interleukin (IL)-12, Interferon (IFN), IL-4, IL-10, and Tumor necrosis factor (TNF)-alpha will be examined. Signaling initiated from IL-12, IFN-gamma and TNF-alpha are important for inducing Th1 responses, and on the other hand signaling from IL-4 and IL-10 receptors inhibit Th1 responses. We will also discuss human immunodeficiencies resulting from mutations in the genes that encode the Type I cytokine receptors.

L11 ANSWER 2 OF 973 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:468655 BIOSIS
DN PREV200200468655
TI [Tumor necrosis factor: Signal transduction pathways, molecular mechanisms of expression and role in pathogenesis of inflammatory disorders and lymphomas. Part I.
Original Title: Czynnik martwicy nowotworow: Przekazywanie sygnalu wewnatrzkomorkowego, molekularne mechanizmy ekspresji i udzial w patogenezie chorob zapalnych i chloniakow. Czesc I..
AU Juszczynski, Przemyslaw (1); Warzocha, Krzysztof (1)
CS (1) Klinika Hematologii, AM w Lodzi, ul Ciolkowskiego 2, 93-510, Lodz Poland
SO Acta Haematologica Polonica, (2002) Vol. 33, No. 2, pp. 191-203. print.
ISSN: 0001-5814.
DT Article
LA Polish
AB Tumor necrosis factor (TNF) plays a crucial role in normal ontogenesis and function of the immune system. Signal transduction pathways which are initiated by ***TNF*** utilize membrane ***receptors*** type I (p55) and II (p75) and terminate on cellular apoptosis or proliferation. The first part of the ***review*** deals with molecular mechanisms of signal transduction pathways induced by TNF. The second part describes its molecular mechanisms of expression and role in pathogenesis of inflammatory disorders and lymphomas.

L11 ANSWER 3 OF 973 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:403707 BIOSIS
DN PREV200200403707
TI Local immunotherapy with rhTNF-alpha mutein induces strong antitumor activity without overt toxicity: A ***review*** .
AU Terlikowski, Slawomir J. (1)
CS (1) Department of Pathophysiology of Pregnancy, Medical Academy of Bialystok, M.C. Sklodowskiej 24A, 15-276, Bialystok: ster@zeus.amb.edu.pl Poland
SO Toxicology, (June 5th, 2002) Vol. 174, No. 3, pp. 143-152. http://www.elsevier.com/locate/toxicol. print.
ISSN: 0300-483X.
DT Article; General Review
LA English
AB Tumor necrosis factor (TNF-alpha) is a cytokine possessing antitumor and immunomodulatory properties. The studies reviewed in the present paper evaluate the effect of intratumor or intraperitoneal (i.t./i.p.) injections of human recombinant TNF-alpha (rhTNF-alpha) and its derivatives (muteins V and VI) on the course of experimental tumors. The aim of local cytokine administration was to avoid or reduce the induction of undesired systemic symptoms. Although total remissions were not observed in the studies, morphological analysis of lung tissue, accepted as the toxicity index of the cytokines, showed that rhTNF-alpha produced the least side effects. Mutein V selectively binds to p55R receptor and at the same time exhibits high antitumor activity. These results confirm the usefulness of studies on the structurally altered rhTNF-alpha derivatives, produced by means of genetic engineering techniques, which bind selectively to different cellular ***receptors*** of ***TNF*** -alpha and show similar or stronger antitumor activity compared with a native molecule, without inducing undesired symptoms.

L11 ANSWER 4 OF 973 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:296624 BIOSIS
DN PREV200200296624
TI Cytotoxic signal transmission pathways via ***TNF*** family ***receptors*** .
AU Beletsky, I. P. (1); Moshnikova, A. B.; Prusakova, O. V.
CS (1) Institute of Theoretical and Experimental Biophysics, Russian Academy of Sciences, ul. Institutskaya 3, Pushchino, Moscow Region, 142290: beletsky@venus.iteb.serpukhov.su Russia
SO Biochemistry (Moscow), (March, 2002) Vol. 67, No. 3, pp. 312-328. http://www.maik.rssi.ru/cgi-bin/journal.pl?name=biochmsc&page=main. print.
ISSN: 0006-2979.
DT General Review
LA English
AB Studies indicating an important role of the ***TNF*** - ***receptor*** family in control of cell proliferation, differentiation, and death have drastically increased in number in recent years. The main function of many members of this family is cell death triggering, and this is apparently the only function for some of them. Studies on the molecular mechanisms of cell death activated by members of the ***TNF*** - ***receptor*** family revealed and identified proteins directly or indirectly associated with ***TNF*** ***receptors*** . Pathways of cytotoxic signal transduction by some members of the TNF-Rs family based on currently proven protein-protein interactions and the role of distinct proteins in these processes are summarized in this ***review*** .

L11 ANSWER 5 OF 973 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:269684 BIOSIS
DN PREV200200269684
TI Activation-induced cell death: The controversial role of Fas and Fas ligand in immune privilege and tumour counterattack.
AU Maher, Stephen; Toomey, Deirdre (1); Condron, Claire; Bouchier-Hayes, David
CS (1) Department of Surgery, RCSI Education and Research Centre, Beaumont Hospital, Dublin 9: toomeydeirdre@hotmail.com Ireland
SO Immunology and Cell Biology, (April, 2002) Vol. 80, No. 2, pp. 131-137. http://www.blackwell-science.com/ cgilib/jnlpage.asp?Journal=xicb&File=xicb. print.
ISSN: 0818-9641.
DT General Review
LA English
AB Activation-induced cell death (AICD) is the process by which cells undergo apoptosis in a controlled manner through the interaction of a death factor and its receptor. Programmed cell death can be induced by a number of physiological and pathological factors including Fas (CD95)-Fas ligand (FasL/CD95L) interaction, tumour necrosis factor (TNF), ceramide, and reactive oxygen species (ROS). Fas is a 48-kDa type I transmembrane protein that belongs to the ***TNF*** /nerve growth factor ***receptor*** superfamily. FasL is a 40-kDa type II transmembrane protein that belongs to the TNF superfamily. The interaction of Fas with FasL results in a series of signal transductions which initiate apoptosis. The induction of apoptosis in this manner is termed AICD. Activation-induced cell death and Fas-FasL interactions have been shown to play significant roles in immune system homeostasis. In this ***review*** the involvement of Fas and Fas ligand in cell death, with particular reference to the T cell, and the mechanism(s) by which they induce cell death is described. The role of AICD in immune system homeostasis and the controversy surrounding the role of FasL in immune privilege, inflammation, and so-called tumour counterattack is also discussed.

L11 ANSWER 6 OF 973 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:268294 BIOSIS
DN PREV200200268294
TI ***TNF*** ***receptor*** subtype signalling: Differences and cellular consequences.
AU MacEwan, David J. (1)
CS (1) Department of Biomedical Sciences, Institute of Medical Sciences, University of Aberdeen, AB25 2ZD, Aberdeen: david.macewan@abdn.ac.uk UK
SO Cellular Signalling, (June, 2002) Vol. 14, No. 6, pp. 477-492. http://www.elsevier.com/locate/cellsig. print.
ISSN: 0898-6568.
DT General Review
LA English
AB Tumour necrosis factor-alpha (TNFalpha) is a multifunctional cytokine belonging to a family of ligands with an associated family of receptor

proteins. The pleiotropic actions of TNF range from proliferative responses such as cell growth and differentiation, to inflammatory effects and the mediation of immune responses, to destructive cellular outcomes such as apoptotic and necrotic cell death mechanisms. Activated ***TNF*** ***receptors*** mediate the association of distinct proteins that regulate a variety of signalling processes including kinase or phosphatase activation, lipase stimulation, and protease induction. Moreover, the cytokine regulates the activities of transcription factors, heterotrimetric or monomeric G-proteins and calcium ion homeostasis in order to orchestrate its cellular functions. This ***review*** addresses the structural basis of TNF signalling, the pathways employed with their cellular consequences, and functions. This ***review*** addresses the structural basis of TNF signalling, the pathways employed with their cellular consequences, and focuses on the specific role played by each of the two ***TNF*** ***receptor*** isotypes, TNFR1 and TNFR2.

L11 ANSWER 7 OF 973 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:112982 BIOSIS
DN PREV200200112982
TI Tissue inhibitors of metalloproteinases and programmed cell death: Conundrums, controversies and potential implications.
AU Mannello, F. (1); Gazzanelli, G.
CS (1) Facolta di Scienze MFN, Istituto di Istologia e Analisi di Laboratorio, Universita degli Studi, Via Zeppi, 61029, Urbino, PU: mannello@uniurb.it Italy
SO Apoptosis, (December, 2001) Vol. 6, No. 6, pp. 479-482. print.
ISSN: 1360-8185.
DT Article
LA English
AB Matrix metalloproteinases (MMPs) are a family of zinc-dependent endopeptidases, which can synergistically degrade the major components of extracellular matrix (ECM). A key role in maintaining the balance between ECM deposition and degradation in several physio-pathological processes is carried out, through multiple biological functions, by four members of the tissue inhibitors of metalloproteinases (TIMPs) family. TIMP-1 and TIMP-2 are capable of inhibiting the activities of MMPs, can inhibit tumour growth, invasion and metastasis, exhibit growth factor-like activity, can inhibit angiogenesis and suppress programmed cell death (PCD) independently of the MMP-inhibitory activity. TIMP-3 is the only member which is tightly bound to ECM, inhibits TNF-alpha converting enzyme and induces PCD through the stabilization of ***TNF*** -alpha ***receptors*** on the cell surface. TIMP-4 plays a role in ECM homeostasis in a tissue-specific fashion and its overexpression induces PCD. The aim of this article is to ***review*** the exciting and intriguing literature on TIMPs, with special emphasis on their conflicting-paradoxical roles in PCD and their potential clinical usefulness.

L11 ANSWER 8 OF 973 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:10050 BIOSIS
DN PREV200200010050
TI Molecular mechanisms of CD40 signaling.
AU Bishop, Gail A. (1); Hostager, Bruce S.
CS (1) Immunology Graduate Program, The University of Iowa, 3-570 Bowen Science Bldg., Iowa City, IA, 52242: gail-bishop@uiowa.edu USA
SO Archivum Immunologiae et Therapiae Experimentalis, (2001) Vol. 49, No. 2, pp. 129-137. print.
ISSN: 0004-069X.
DT General Review
LA English
AB CD40, a member of the growing tumor necrosis factor ***receptor*** (***TNF*** -R) family of molecules, functions as a transmembrane signal receptor in both hematopoietic and non-hematopoietic cell types, although its physiological roles are less well understood in the latter. Much has been learned over the past decade about the role of CD40 signaling in various cellular functions. In addition, some of the molecular events which occur subsequent to CD40 engagement have been characterized, although much remains to be understood. This ***review*** will summarize the known important biological roles of CD40, and discuss what is currently known about how CD40 signals.

L11 ANSWER 9 OF 973 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:515966 BIOSIS
DN PREV200100515966
TI Evidence for a pro-apoptotic function of CD137 in granulocytes.
AU Simon, Hans-Uwe (1)
CS (1) Dept. of Pharmacology, University of Bern, Friedbuhlstrasse 49, CH-3010, Bern: hus@pki.unibe.ch Switzerland
SO Swiss Medical Weekly, (August, 2001) Vol. 131, No. 31-32, pp. 455-458. print.
ISSN: 1424-7860.
DT General Review
LA English
SL English
AB Granulocyte apoptosis is crucial for control ling granulocyte number under normal and inflammatory conditions. Reduced apoptosis of different types of granulocytes is one important mechanism for cell accumulation. Which granulocyte subtype expands is largely dependent on the cytokine milieu present at the inflammatory site. Over expression of G-CSF and GM-CSF is associated with neutrophilia, whereas over expression of IL-5 is linked to eosinophilia. Cytokine withdrawal leads to the induction of granulocyte apoptosis, a mechanism which occurs during resolution of inflammation. Besides survival factors, granulocyte apoptosis is also regulated by death factors, which belong to the tumor necrosis factor (TNF)/nerve growth factor (NGF) superfamily. Recent observations suggest that granulocytes can be activated via CD137, a member of the ***TNF*** /NGF ***receptor*** superfamily. This ***review*** summarizes our current knowledge on the potential role of CD137 in the regulation of both neutrophil and eosinophil apoptosis.

L11 ANSWER 10 OF 973 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:483033 BIOSIS
DN PREV200100483033
TI Crosstalk between NF-kappaB-activating and apoptosis-inducing proteins of the ***TNF*** - ***receptor*** complex.
AU Heyninck, Karen; Beyaert, Rudi (1)
CS (1) Unit for Molecular Signal Transduction in Inflammation, Department of Molecular Biology, University of Ghent, K. L. Ledeganchkstraat 35, B-9000, Ghent: rudi.beyaert@DMB.RUG.AC.BE Belgium
SO Molecular Cell Biology Research Communications, (September, 2001) Vol. 4, No. 5, pp. 259-265. print.
ISSN: 1522-4724.
DT General Review
LA English
SL English
AB The cytokine tumor necrosis factor (TNF) elicits a wide range of biological responses, including inflammation, cell proliferation, differentiation, and apoptosis. Although the molecular mechanisms of TNF signaling have been largely elucidated, the principle that regulates the balance of life and death is still unknown. This ***review*** will focus on the crosstalk that exists between proteins of the ***TNF*** ***receptor*** (***TNF*** -R) signalosome, and which are involved in the initiation of nuclear factor kappa B (NF-kappaB) activation or apoptosis. At least four different mechanisms of regulation can be distinguished: (i) NF-kappaB-mediated induction of proteins of the TNF-R complex; (ii) NF-kappaB-independent protection against apoptosis by the TNF-R-associating factor 2 (TRAF2)-mediated recruitment of anti-apoptotic proteins; (iii) dual activation of apoptosis and NF-kappaB by a single molecule; and (iv) amplification of the death signal by proteolytic inactivation of signaling proteins that are involved in NF-kappaB activation or cell survival.

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CA SUBSCRIBER PRICE 0.00 -2.48

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FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 14:56:17 ON 06 NOV 2002
L1 1 S TNF RECEPTOR ASSOCIATED WITH DEATH PROTEIN? OR TNF RECEPTOR A
L2 3 S TRADE ALPHA OR TRADE BETA

L3 3 DUP REM L2 (0 DUPLICATES REMOVED)
L4 599 S TNF RECEPTOR FAMIL?
L5 2 S L4 AND TRADE
L6 2 DUP REM L5 (0 DUPLICATES REMOVED)
L7 0 S L6 NOT L3
L8 2 S OAF065
L9 2 DUP REM L8 (0 DUPLICATES REMOVED)
L10 12584 S TNF (3A) RECEPTOR?
L11 973 S L10 AND REVIEW

FILE 'STNGUIDE' ENTERED AT 15:17:48 ON 06 NOV 2002

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 15:22:21 ON 06 NOV 2002

=> s l10 and trade
L12 3 L10 AND TRADE

=> dup rem l12
PROCESSING COMPLETED FOR L12
L13 3 DUP REM L12 (0 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 3 ANSWERS - CONTINUE? Y/(N):y

L13 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2002 ACS
AN 2001:598038 CAPLUS
DN 135:175423
TI ***TRADE*** molecules and uses related thereto
IN Wood, Clive; Chaudhary, Divya; Long, Andrew
PA Genetics Institute, Inc., USA
SO PCT Int. Appl., 173 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001058954	A2	20010816	WO 2001-US4238	20010209
WO 2001058954	A3	20020321		

PI W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
US 2002068696 A1 20020606 US 2001-780532 20010209
PRAI US 2000-181922P P 20000211
US 2000-182148P P 20000214
AB The present invention relates, at least in part, to methods of modulating proliferation and apoptotic state of cells using agents that modulate the expression and/or activity of ***TRADE*** family polypeptides. In addn., the invention provides two novel members of the ***TRADE*** family of mols.

L13 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:408685 BIOSIS
DN PREV200000408685
TI ***TRADE*** : A novel ***TNF*** - ***receptor*** family member.
AU Long, Andrew J. (1); Bourque, Karen (1); Chaudhary, Divya (1); Haga, Hisanori; Tada, Hideaki; Burgess, Paul (1); Whitters, Matthew (1); Tan, Xiang Yan (1); O'Hara, Denise (1); Fitz, Lori (1); Beier, David; McCoy, John (1); Collins, Mary (1); Shibayama, Shiro; Wood, Clive R. (1)
CS (1) Genetics Institute, Inc., Wyeth Ayerst Research, Cambridge, MA, 02140 USA
SO Scandinavian Journal of Immunology, (June, 2000) Vol. 51, No. Supplement 1, pp. 64. print.
Meeting Info.: 8th International TNF Congress, Conference on Tumor Necrosis Factor and Related Molecules Scientific Advances and Medical Applications Trondheim, Norway May 14-18, 2000
ISSN: 0300-9475.
DT Conference
LA English
SL English

L13 ANSWER 3 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:377034 BIOSIS
DN PREV200000377034
TI ***TRADE*** , a novel ***TNF*** ***receptor*** superfamily member, induces apoptosis and activates NFkappaB and Jnk.
AU Chaudhary, Divya (1); Long, Andrew J. (1); Bourque, Karen (1); Adams, David H.; Hubscher, Stefan G.; Towler, Paul (1); Potts, Douglas (1); Wood, Clive R. (1)
CS (1) Genetics Institute, Inc., Wyeth Ayerst Research, 87 Cambridge Park Drive, Cambridge, MA, 02140 USA
SO Scandinavian Journal of Immunology, (June, 2000) Vol. 51, No. Supplement 1, pp. 33. print.
Meeting Info.: 8th International TNF Congress, Conference on Tumor Necrosis Factor and Related Molecules Scientific Advances and Medical Applications Trondheim, Norway May 14-18, 2000
ISSN: 0300-9475.
DT Conference
LA English
SL English

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L2 3 S TRADE ALPHA OR TRADE BETA
L3 3 DUP REM L2 (0 DUPLICATES REMOVED)
L4 599 S TNF RECEPTOR FAMIL?
L5 2 S L4 AND TRADE
L6 2 DUP REM L5 (0 DUPLICATES REMOVED)
L7 0 S L6 NOT L3
L8 2 S OAF065
L9 2 DUP REM L8 (0 DUPLICATES REMOVED)
L10 12584 S TNF (3A) RECEPTOR?
L11 973 S L10 AND REVIEW

FILE 'STNGUIDE' ENTERED AT 15:17:48 ON 06 NOV 2002

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 15:22:21 ON 06 NOV 2002
L12 3 S L10 AND TRADE
L13 3 DUP REM L12 (0 DUPLICATES REMOVED)

=> s l11 and (cell prolifer? or cell death)
L14 187 L11 AND (CELL PROLIFER? OR CELL DEATH)

=> dup rem l14
PROCESSING COMPLETED FOR L14
L15 134 DUP REM L14 (53 DUPLICATES REMOVED)

=> s l10 and NFkB
L16 36 L10 AND NFKB

=> dup rem l16
PROCESSING COMPLETED FOR L16
L17 30 DUP REM L16 (6 DUPLICATES REMOVED)

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YOU HAVE REQUESTED DATA FROM 30 ANSWERS - CONTINUE? Y/(N):y

L17 ANSWER 1 OF 30 CAPLUS COPYRIGHT 2002 ACS
AN 2002:615681 CAPLUS
DN 137:168284
TI TR430 receptor protein and antibodies for treating NF-.kappa.B-associated diseases
IN Yoshida, Kenji; Oda, Tsukasa; Koga, Hisashi; Masuho, Yasuhiko; Isogai, Takao
PA Helix Research Institute Inc., Japan
SO PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002062852	A1	20020815	WO 2002-JP927	20020205

PI W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI JP 2001-28725 A 20010205
JP 2001-303223 A 20010928
AB Disclosed is an antibody specifically binding to TR430 proteins (i.e. TR430a and TR430g proteins, while both belong to ***TNF*** ***receptor*** family) or analogs thereof. The antibody is used for screening test compds. regulating the NF-kB transcriptional activity in cells wherein a TR430 protein is expressed. Compds. obtained by this method and medicinal compns. contg. the above antibody or the compd. obtained by the above screening method are useful for treating diseases relating to an increase or a decrease in the NF-kB activity in cells.

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 2 OF 30 CAPLUS COPYRIGHT 2002 ACS
AN 2002:157943 CAPLUS
DN 136:194280
TI TRANCE regulation of chondrocyte differentiation
IN Choi, Yongwon; Odgren, Paul R.; Marks, Sandy C., Jr.
PA University of Massachusetts Medical Center, USA
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002016551	A2	20020228	WO 2001-US26101	20010820
AU 2001086586	A5	20020304	AU 2001-86586	20010820
PRAI US 2000-226197P	P	20000818		
WO 2001-US26101	W	20010820		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AB Disclosed are therapeutic methods of treating a mammal, e.g., a human patient, having a disease, disorder or condition characterized by abnormal (excessive or insufficient) cartilage growth or skeletal growth. The methods include inhibiting or supplementing activity of TRANCE or TRAF6 in chondrocytes in vivo or ex vivo. Also disclosed are methods of diagnosing a cartilage disorder. The method includes detecting an elevated or reduced level of TRANCE, RANK, or TRAF6 in chondrocytes. Also disclosed are methods of identifying a compd. that increases or decreases proliferation of chondrocytes, or a compd. that promotes differentiation, e.g., maturation, of chondrocytes. A TRANCE knockout mouse was generated which was then rescued by a TRANCE transgene under the control of a lymphocyte-specific promoter.

L17 ANSWER 3 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
AN 2002:259147 BIOSIS
DN PREV200200259147
TI Osteoclast induction in periodontal tissue during experimental movement of incisors in osteoprotegerin-deficient mice.
AU Oshiro, Takahiro; Shiotani, Aya; Shibasaki, Yoshinobu; Sasaki, Takahisa (1)
CS (1) Department of Oral Histology, School of Dentistry, Showa University, 1-5-8 Hatanodai, Shinagawa-ku, Tokyo, 142-8555: oralhist@dent.showa-u.ac.jp Japan
SO Anatomical Record, (April 1, 2002) Vol. 266, No. 4, pp. 218-225. http://www.interscience.wiley.com/jpages/0003-276X/. print. ISSN: 0003-276X.
DT Article
LA English
AB Osteoprotegerin (OPG) is a novel secreted member of the tumor necrosis factor (***TNF***) ***receptor*** superfamily that negatively regulates osteoclastogenesis. The receptor activator of the ***NFKB*** ligand (RANKL) is one of the key regulatory molecules in osteoclast formation and binds to OPG. In this study, it was suggested that OPG and RANKL are involved in alveolar bone remodeling during orthodontic tooth movement. We examined RANKL localization and osteoclast induction in periodontal tissues during experimental movement of incisors in OPG-deficient mice. To produce orthodontic force, an elastic band was inserted between the upper right and left incisors for 2 or 5 days, and the dissected maxillae were examined for cytochemical and immunocytochemical localization of tartrate-resistant acid phosphatase (TRAP), vacuolar-type H+-ATPase, and RANKL. Compared to wild-type OPG (+/+) littermates, TRAP-positive multinucleated cells were markedly induced in the periodontal ligament (PDL) on the compressed side and in the adjacent alveolar bone of OPG-deficient mice. These multinucleated cells exhibited intense vacuolar-type H+-ATPase along the ruffled border membranes. Because of accelerated osteoclastic resorption in OPG-deficient mice, alveolar bone was severely destroyed and partially perforated at 2 and 5 days after force application. In both wild-type and OPG-deficient mice, RANKL expression became stronger at 2 and 5 days after force application than before force application. There was no apparent difference in intensity of RANKL expression between OPG (+/+) littermates and OPG-deficient mice. In both wild-type and OPG-deficient mice, expression of RANKL protein was detected in osteoblasts, fibroblasts, and osteoclasts mostly located in resorption lacunae. These results suggest that during orthodontic tooth movement, RANKL and OPG in the periodontal tissues are important determinants regulating balanced alveolar bone resorption.

L17 ANSWER 4 OF 30 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 2
AN 2002350317 EMBASE
TI Regulation of osteoclast differentiation and function by receptor activator of ***NFkB*** ligand and osteoprotegerin.
AU Shiotani A.; Takami M.; Itoh K.; Shibasaki Y.; Sasaki T.
CS T. Sasaki, Department of Oral Histology, School of Dentistry, Showa University, 1-5-8 Hatanodai, Shinagawa-ku, Tokyo 142-8555, Japan. oralhist@dent.showa-u.ac.jp
SO Anatomical Record, (1 Oct 2002) 268/2 (137-146).
Refs: 25
ISSN: 0003-276X CODEN: ANREAK
CY United States
DT Journal; Article
FS 001 Anatomy, Anthropology, Embryology and Histology
029 Clinical Biochemistry
LA English
SL English
AB The differentiation and functions of osteoclasts (OCs) are regulated by osteoblast-derived factors. Receptor activator of ***NFkB*** ligand (RANKL) is one of the key regulatory molecules in OC formation. Osteoprotegerin (OPG) is a novel secreted member of the ***TNF*** ***receptor*** superfamily that negatively regulates osteoclastogenesis and binds to RANKL. We examined the biological actions of macrophage-colony-stimulating factor (M-CSF), RANKL, and OPG on the differentiation of OCs isolated from cocultures of mouse osteoblastic cells and bone marrow cells. Preosteoclasts (pOCs) and OCs were characterized by their ultrastructure and the expression of OC markers such as tartrate-resistant acid phosphatase (TRAP) and vacuolar-type H(+)-ATPase. pOCs formed without any additives expressed TRAP, but showed little resorptive activity on cocultured dentine slices. TRAP-positive pOCs treated with M-CSF began to fuse with each other, but lacked a ruffled border (RB) and showed almost no resorptive activity. pOCs treated with RANKL became TRAP-positive multinucleated cells, which expressed intense vacuolar-type H(+)-ATPase along the RB membranes and exhibited prominent resorptive activity. Such effects of RANKL on pOCs were completely inhibited by the addition of OPG. OPG inhibited RB formation in mature OCs and reduced their resorptive activity, and also induced apoptosis of some OCs. These results suggest that 1) RANKL induces differentiation of functional OCs from pOCs, 2) M-CSF induces macrophage-like multinucleated cells, but not OCs, 3) OPG inhibits RB formation and resorptive activity in mature OCs, 4) OPG also induces apoptosis of OCs, and 5) RANKL and OPG are, therefore, important regulators of not only the terminal differentiation of OCs but also their resorptive function. .COPYRGT. 2002 Wiley-Liss, Inc.

L17 ANSWER 5 OF 30 CAPLUS COPYRIGHT 2002 ACS
AN 2002:318112 CAPLUS
DN 137:166749
TI Stable Inhibition of NF-.kappa.B in Salivary Gland Cells Does Not Enhance Sensitivity to TNF-.alpha.-Induced Apoptosis Due to Upregulation of TRAF-1 Expression
AU Aota, Keiko; Azuma, Masayuki; Tamatani, Tetsuya; Yamashita, Tsuyoshi; Ashida, Yuki; Sato, Mitsunobu
CS Second Department of Oral and Maxillofacial Surgery, Tokushima University School of Dentistry, Tokushima, 770-8504, Japan
SO Experimental Cell Research (2002), 276(1), 111-119
CODEN: ECREAL; ISSN: 0014-4827
PB Elsevier Science
DT Journal
LA English
AB The transcription factor NF-.kappa.B inhibits the apoptotic response induced by TNF-.alpha.. However, in salivary gland cell clones (ACMT-6 and ACMT-7) in which NF-.kappa.B activation was suppressed by introduction of a super-repressor form of I.kappa.B-.alpha. cDNA, TNF-.alpha. did not cause apoptosis. Thus, to investigate the mol. mechanism involved in the unresponsiveness of these cell clones to TNF-.alpha.-induced apoptosis, we examd. the effect of TNF-.alpha. on the expression of antiapoptotic proteins, including ***TNF*** ***receptor*** -assocd. factor (TRAF)-1, TRAF-2, cellular inhibitor of apoptosis protein (cIAP)-1, and cIAP-2. Here we show that expression of TRAF-1 was commonly detected by treatment with TNF-.alpha. in ACMT-6, ACMT-7, and an empty vector-transfected cell clone (ACpRc-1) and that downregulation of TRAF-1 protein by either treatment with an antisense oligonucleotide or introduction of an antisense plasmid resulted in the induction of apoptosis in these cell clones. Our results, therefore, suggest that one of the mechanisms by which cells acquire resistance to TNF-.alpha.-induced apoptosis is a TNF-.alpha. induction of TRAF-1.
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 6 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:209107 BIOSIS
DN PREV200200209107
TI Recent advances in understanding of the molecular basis of anhidrotic ectodermal dysplasia: Discovery of a ligand, ectodysplasin A and its two receptors.
AU Wisniewski, Slawomir A.; Kobielak, Agnieszka; Trzeciak, Wieslaw H. (1); Kobielak, Krzysztof
CS (1) Department of Biochemistry and Molecular Biology, ul. Swiecickiego 6, 60-781, Poznan: trzeciak@am.poznan.pl Poland
SO Journal of Applied Genetics, (2002) Vol. 43, No. 1, pp. 97-107. print. ISSN: 1234-1983.
DT General Review

LA English
AB Recent developments of the investigations on the molecular basis of anhidrotic ectodermal dysplasia are reviewed. Identification of the major product of the EDA gene (ectodysplasin A), a protein belonging to a group of TNF ligands, and molecular cloning of the cDNA, encoding its receptor (EDAR), a member of the ***TNF*** ***receptor*** family, are presented. The role of an alternative EDA receptor, localised on the X chromosome (XEDAR) in the developmental control of the differentiation of skin appendages, is discussed. Recent findings have elucidated the cause of the autosomal forms of EDA, both dominant and recessive, and indicated an important role of a signal transduction pathway involving a protein product of the NEMO gene and the transcription factor NFkappaB in the differentiation of skin appendages.

L17 ANSWER 7 OF 30 CAPLUS COPYRIGHT 2002 ACS
AN 2002:365132 CAPLUS
DN 137:107716
TI Role of reactive oxygen species in NF-.kappa.B signaling
AU Hayakawa, Makio
CS Sch. Pharm., Tokyo Univ. Pharm. Life Sci., Tokyo, 192-0392, Japan
SO Yakugaku Kenkyu no Shinpo (2002), 18, 95-104
CODEN: YAKSEY; ISSN: 0914-4544
PB Yakugaku Kenkyu Shorei Zaidan
DT Journal; General Review
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 10141236	A1	20020516	DE 2001-10141236	20010823
US 2002077404	A1	20020620	US 2001-931963	20010816
JP 2002146134	A2	20020522	JP 2001-297714	20010927

PRAI KR 2000-64688 A 20001101
AB A review. Nuclear factor kappa B (NF-.kappa.B)/Rel proteins are dimeric, sequence-specific transcription factors involved in the activation of a large no. of genes in response to inflammation, viral and bacterial infections, and other stressful situations requiring rapid reprogramming of gene expression. In resting cells, NF-.kappa.B proteins are sequestered in the cytoplasm through their assocn. with members of the I.kappa.B (inhibitor of NF-.kappa.B) family of inhibitor proteins. Upon stimulation, I.kappa.B is rapidly phosphorylated, polyubiquitinated, and then degraded by 26S proteasome. Once feed from I.kappa.B, NF-.kappa.B translocates to the nucleus, where it activates the transcription of its specific target genes. Among several antioxidants, N-acetylcysteine (NAC) and pyrrolidine dithiocarbamate (PDTC) are known to inhibit NF-.kappa.B activation. However, the mol. mechanism of their inhibitory action is not fully elucidated. NAC strongly inhibited tumor necrosis factor (TNF)-induced activation of I.kappa.B kinase (IKK) which leads to the activation of NF-.kappa.B. Furthermore, NAC also blocked the TNF-induced activation of three mitogen activated protein (MAP) kinases, c-Jun N-terminal kinase (JNK), p38, and extracellular signal-regulated kinase (ERK). In contrast, 12-O-tetradecanoylphorbol-13-acetate (TPA) and interleukin-1 (IL-1)-induced activation of these signaling pathways were not affected by the treatment with NAC. On the other hands, PDTC sufficiently blocked TNF-, IL-1-, and TPA-induced activation of NF-.kappa.B and JNK. However, PDTC augmented p38 and ERK activation induced by TNF and IL-1. To clarify which step of the signaling cascade is affected by the treatment with these compds., the recruitment of the ***TNF*** ***receptor*** -assocd. factor 2 (TRAF2) and the death domain kinase RIP (***receptor*** interacting protein) to ***TNF*** ***receptor*** 1 (***TNF*** -R1) was examd. The pretreatment of cells with NAC significantly inhibited the recruitment of TRAF2 and RIP to TNF-R1. In contrast, PDTC pretreatment did not change the recruitment of these mols. to TNF-R1. This result suggest that NAC blockes the initial step of TNF-R1 activation whereas PDTC targets at steps downstream of TNF-R1/TRAF2/RIP signaling complex. Moreover, we demonstrated that NAC treatment decreased the affinity of ***TNF*** ***receptor*** toward 125I- ***TNF*** . These results indicate the distinct mechanism of inhibition by NAC and PDTC toward TNF-activated NF-.kappa.B and JNK pathway and raise the question of whether or not these inhibitors act simply as antioxidants. Furthermore, NADPH oxidase, a possible candidate which produce reactive oxygen species (ROS) in response to TNF, was not involved in TNF-stimulated NF-.kappa.B activation. Therefore, it is unlikely that ROS act as the second messenger in NF-.kappa.B signaling.

L17 ANSWER 8 OF 30 CAPLUS COPYRIGHT 2002 ACS
AN 2001:397044 CAPLUS
DN 134:362290
TI Cloning of human ***TNF*** ***receptor*** R248 cDNA and its use in the treatment of immune disorders
IN Kitson, Jeremy David Alistair
PA Glaxo Group Limited, UK
SO PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001038526	A1	20010531	WO 2000-GB4438	20001121

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI GB 1999-27681 A 19991123
AB A novel ***TNF*** ***receptor*** R248 is provided which is a screening target for the identification and development of novel pharmaceutical agents which modulate the activity of the receptor and in particular modulate activation of NF.kappa.B by the receptor. The present invention provides the cDNA sequences coding for human ***TNF*** - ***receptor*** R248 polypeptide. A method for identification of a substance that modulates ***TNF*** ***receptor*** activity comprises contacting a polypeptide of the invention with a test substance in the presence of a reporter whose activity is mediated by ***NFkB*** and monitoring ***NFkB*** mediated activity.
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 9 OF 30 CAPLUS COPYRIGHT 2002 ACS
AN 2001:870075 CAPLUS
DN 136:33180
TI Additive activation of hepatic NF-.kappa.B by ethanol and HBX or HCV core protein: involvement of ***TNF*** -.alpha. ***receptor*** I-independent and -dependent mechanisms
AU Kim, Won-Ho; Hong, Feng; Jaruga, Barbara; Hu, Zongyi; Fan, Saijun; Liang, T. Jake; Gao, Bin
CS Section on Liver Biology, Laboratory of Physiologic Studies, National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health, Bethesda, MD, USA
SO FASEB Journal (2001), 15(13), 2551-2553, 10.1096/fj.00-01-217fje
CODEN: FAJOEC; ISSN: 0892-6638
PB Federation of American Societies for Experimental Biology
DT Journal
LA English
AB Alc. consumption and viral hepatitis infection synergistically accelerate liver injury, but the underlying mechanism is not fully understood. Here the authors have examd. the effects of ethanol on hepatitis B protein X (HBX)- or hepatitis C core protein (HCV core protein)-mediated activation of NF-KB. a crit. signal in hepatic injury, regeneration, and tumor transformation. Acute ethanol or acetaldehyde exposure potentiates HBX or HCV core protein activation of NF-.kappa.B in primary mouse hepatocytes. Such potentiation can be abolished by blocking ethanol metab. or overexpression of dominant neg. NF-.kappa.B-inducing kinase (NIK), IKB kinase (IKK), or IKB. Moreover, pertussis toxin attenuates NF-.kappa.B activation induced by acetaldehyde but not by HBX or HCV core protein, whereas HBX or HCV core protein-mediated activation of NF-.kappa.B is abolished completely in tumor necrosis factor .alpha. receptor 1 (TNFRI) (-/-) hepatocytes. Finally, chronic ethanol consumption induces hepatic CYP2E1 protein expression and potentiates HBX or HCV core protein activation of NF-.kappa.B in the liver. These findings suggest that ethanol activates hepatic NF-.kappa.B via its metab. and that HBX or HCV core protein activates hepatic NF-.kappa.B via TNFR1. With the essential role of TNFR1 in alc. liver injury, targeting TNFR1 by hepatitis viral proteins could contribute to cooperative effects of alc. consumption and viral hepatitis on liver disease.
RE.CNT 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 10 OF 30 CAPLUS COPYRIGHT 2002 ACS
AN 2001:870090 CAPLUS
DN 136:132203
TI CD40 activation-induced, Fas-dependent apoptosis and NF-.kappa.B/AP-1 signaling in human intrahepatic biliary epithelial cells
AU Afford, Simon C.; Ahmed-Choudhury, Jalal; Randhawa, Satinder; Russell, Clare; Youster, Janine; Crosby, Heather A.; Eliopoulos, Aristides; Hubscher, Stefan G.; Young, Lawrence S.; Adams, David H.
CS Liver Research Laboratories, MRC Centre for Immune Regulation, and The Department of Pathology, The University of Birmingham, Birmingham, B15 2TH, UK
SO FASEB Journal (2001), 15(13), 2345-2354
CODEN: FAJOEC; ISSN: 0892-6638
PB Federation of American Societies for Experimental Biology
DT Journal
LA English
AB Fas-mediated mechanisms of apoptosis are thought to be involved in the bile duct loss that characterizes diseases such as primary biliary cirrhosis (PBC). We have previously shown that activation of CD40 on hepatocytes can amplify Fas-mediated apoptosis; in the present study, we investigated interactions between CD40 and Fas in biliary epithelial cells (BEC). We report that the bile ducts in PBC liver tissue frequently express increased levels of Fas, Fas ligand (FasL), and CD40 assocd. with apoptotic BEC. The portal mononuclear infiltrate contains CD40L+ve T cells and macrophages, thereby demonstrating a potential mechanism for CD40 engagement in vivo. Primary cultures of human BEC also expressed Fas, FasL, and CD40 but not CD40L protein or mRNA. Activation of CD40 on BEC using recombinant CD40L increased transcriptional expression of FasL and induced apoptosis, which was inhibited by neutralizing antibodies to either Fas or FasL. Thus, CD40-induced apoptosis of BEC is mediated through Fas/FasL. We then investigated the intracellular signals and transcription factors activated in BEC and found that NF-KB and AP-1 were

both activated after CD40 ligation. Increased functional NF-KB was seen early after CD40 ligation, but returned to baseline levels after 4 h. In contrast, the rapid up-regulation of AP-I was sustained over 24 h. This study provides further functional evidence of the ability of CD40 to induce Fas/FasL-dependent apoptosis of liver epithelial cells supporting the importance of cross-talk between tumor necrosis factor (***TNF***) ***receptor*** family members as an amplification step in apoptosis induction. Sustained activation of AP-I in the absence of NF-KB signaling may be a crit. factor in detg. the outcome of CD40 engagement.
RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 11 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:557680 BIOSIS
DN PREV200100557680
TI A functional interaction between the p75 associated proteins NRIF and TRAF6.
AU Gentry, J. J. (1); Rutkoski, N. (1); Linggi, M. S. (1); Musiek, E. S. (1); Emeson, R. (1); Carter, B. D. (1)
CS (1) Biochem and Ctr Mol Neurosci, Vanderbilt Univ Med School, Nashville, TN USA
SO Society for Neuroscience Abstracts, (2001) Vol. 27, No. 2, pp. 1825. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001
ISSN: 0190-5295.
DT Conference
LA English
SL English
AB Nerve Growth Factor binding to p75 activates both a survival signal through the transcription factor ***NFkB*** , and cell death through the stress-activated kinase, JNK. NRIF, a protein shown to associate with the intracellular domain of p75, has been implicated in p75-mediated cell death, based on analysis of nrif-/- mice and the induction of apoptosis by ecotopic expression in Schwann cells. Recently, we found that NRIF interacts with TRAF6, a member of the ***TNF*** ***Receptor*** Associated Factor family, which also binds to the ICD of p75. These two p75-binding proteins could be co-immunoprecipitated when expressed in HEK cells. Interestingly, TRAF6 dramatically enhanced NRIF expression, suggesting that the interaction may stabilize NRIF protein. These proteins also functionally interacted, co-expression of NRIF increased TRAF6 activation of ***NFkB*** and JNK 2-3 fold, based on reporter assays. Moreover, when expressed alone Flag-TRAF6 or GFP-NRIF was observed throughout the cytoplasm, including some nuclear distibution of NRIF; however, when co-expressed both proteins localized exclusively in sub-nuclear domains. In contrast, TRAF6 lacking the NH2-terminus, necessary for ***NFkB*** and JNK activation, failed to translocate NRIF. This nuclear localization is particularly interesting since NRIF contains a domain homologous to a transcriptional repressor module and recombinant NRIF can bind specific DNA sequences in gel-shift assays. Taken together, these findings suggest that NRIF and TRAF6 interaction results in maximal activation of downstream signals and nuclear translocation where NRIF can bind DNA, possibly affecting cellular viability by transcriptional repression.

L17 ANSWER 12 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:186454 BIOSIS
DN PREV200200186454
TI Signaling pathway of apoptosis induced by vincristine in acute lymphoblastic leukemia cells: Activation of caspase-2 and downregulation of NF-kB are required for vincristine-induced apoptosis.
AU Zhou, Muxiang (1); Gu, Lubing (1); Findley, Harry W. (1); Woods, William G. (1)
CS (1) Pediatrics, Emory University School of Medicine, Atlanta, GA USA
SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 311a. http://www.bloodjournal.org/. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971.
DT Conference
LA English
AB The process of cancer cell death induced by certain chemotherapeutic agents is apoptosis possibly via distinct pathways, which may differ depending on various agents and different cell types. Here we report that vincristine (VCR), an important drug in chemotherapy of childhood acute lymphoblastic leukemia (ALL), induces apoptosis via a unique signaling pathway different from that induced by DNA-damaging agents, such as ionizing radiation (IR) and doxorubicin (adriamycin), as well as by TNF-alpha. Induction of p53 and activation of caspase-9 that initiate the signal transduction pathway of apoptosis induced by IR and adriamycin were not observed in VCR treated ALL cells. Instead, a specific activation of caspase-2, which executes apoptosis via death ***receptor*** such as ***TNF*** ***receptor*** , was detected in ALL cells treated with VCR. However, activation of NF-kB, which occurs in the treatment of ALL cells with TNF-alpha as well as adriamycin, was not found in ALL cells treated with VCR. In contrast, treatment with VCR significantly reduced NF-kB binding activity in an ALL cell line (EU-1) that has constitutive NF-kB activation. To further evaluate the effect of ***NFkB*** activation on chemotherapeutic agent-induced apoptosis in ALL, we transfected the dominant negative mutant inhibitor of ***NFkB*** (IkBm) into the EU-1 cells. Overexpression of IkBm significantly reduced constitutive ***NFkB*** activity in EU-1 cells, resulting in enhanced sensitivity to VCR- but not adriamycin-induced cell death examined by WST assay. Consistent with increased cell death by VCR in IkBm-transfected EU-1 cells, loss of constitutive ***NFkB*** by transfection of the super repressor significantly enhanced the activation of caspases 2 and 3 and cleavage of its substrate PARP. Therefore, our data indicate that VCR-induced apoptosis is independent of p53 and depends on activation of caspase 2 and downregulation of NF-kB, and suggests that constitutive overexpression of NF-kB in ALL cells from some patients is an important underlying mechanism of resistance to induction therapy with VCR.

L17 ANSWER 13 OF 30 CAPLUS COPYRIGHT 2002 ACS
AN 2000:270255 CAPLUS
DN 133:28857
TI Regulatory mechanisms of TRAF2-mediated signal transduction by Bcl10, a MALT lymphoma-associated protein
AU Yoneda, Takunari; Imaizumi, Kazunori; Maeda, Mitsuyo; Yui, Daishi; Manabe, Takayuki; Katayama, Taiichi; Sato, Naoya; Gomi, Fumi; Morihara, Takashi; Mori, Yasutake; Miyoshi, Ko; Hitomi, Junniti; Ugawa, Shinya; Yamada, Shuichi; Okabe, Masaru; Tohyama, Masaya
CS Department of Anatomy and Neuroscience, Osaka University Medical School, Suita, 565-0871, Japan
SO Journal of Biological Chemistry (2000), 275(15), 11114-11120
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB To elucidate the function of Bcl10, recently cloned as an apoptosis-assocd. gene mutated in MALT lymphoma, we identified its binding partner TRAF2, which mediates signaling via tumor necrosis factor receptors. In mammalian cells, low levels of Bcl10 expression promoted the binding of TRAF2 and c-IAPs. Conversely, excessive expression inhibited complex formation. Overexpressed Bcl10 reduced c-Jun N-terminal kinase activation and induced nuclear factor .kappa.B activation downstream of TRAF2. To det. whether overexpression of Bcl10 could perturb the regulation of apoptosis in vivo, we generated Bcl10 transgenic mice. In these transgenic mice, atrophy of the thymus and spleen was obsd. at postnatal stages. The morphol. changes in these tissues were caused by acceleration of apoptosis in T cells and B cells. The phenotype of Bcl10 transgenic mice was similar to that of TRAF2-deficient mice reported previously, indicating that excessive expression of Bcl10 might deplete the TRAF2 function. In contrast, in the other organs such as the brain, where Bcl10 was expressed at high levels, no apoptosis was detected. The altered sensitivities to overexpressed Bcl10 may have been due to differences in signal responses to Bcl10 among cell types. Thus, Bcl10 was suggested to play crucial roles in the modulation of apoptosis assocd. with TRAF2.
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 14 OF 30 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 2000304002 EMBASE
TI Activation of nuclear factor .kappa.B and induction of apoptosis by tumor necrosis factor-.alpha. in the mouse uterine epithelial WEG-1 cell line.
AU Pampfer S.; Cordi S.; Cikos S.; Picry B.; Vanderheyden I.; De Hertogh R.
CS S. Pampfer, OBST 5330 Research Unit, Univ. Cath. de Louvain Med. Sch., 53 Avenue Mounier, 1200 Brussels, Belgium. pampfer@obst.ucl.ac.be
SO Biology of Reproduction, (2000) 63/3 (879-886).
Refs: 56
ISSN: 0006-3363 CODEN: BIREBV
CY United States
DT Journal; Article
FS 010 Obstetrics and Gynecology
029 Clinical Biochemistry
LA English
SL English
AB In order to better understand how tumor necrosis factor (TNF)-.alpha. may contribute to the local regulation of uterine cell death, cultures of mouse uterine epithelial WEG-1 cells were exposed to TNF-.alpha. and observed at different time intervals. Earliest decrease in cell viability was observed after 31 h of exposure to 50 ng/ml mouse TNF-.alpha. and was associated with the expression of several markers of apoptosis. Treatment with human TNF-.alpha. or addition of a neutralizing antibody against ***TNF*** -.alpha. ***receptor*** protein 80 to mouse TNF-.alpha. resulted in attenuated induction of apoptosis, suggesting that coengagement of the two ***TNF*** -.alpha. ***receptor*** types is required for maximal impact. Ceramide analogs failed to replicate the effect of TNF-.alpha. and the stress-activated protein kinase signaling pathway was not activated by the cytokine. Treatment with mouse TNF-.alpha. resulted in an increase in nuclear factor (NF)kB activity that receded after 24 h. The impact of human TNF-.alpha. on ***NFkB*** activation was more moderate. Addition of either one of three different inhibitors of ***NFkB*** (SN50, PDTC, and A771726) to mouse TNF-.alpha. sensitized WEG-1 cells to the toxicity of the cytokine. Our data suggest that WEG-1 cells initiate their response to TNF-.alpha. with an increase in ***NFkB*** activation that may have transiently biased these cells toward cell death resistance.

L17 ANSWER 15 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:418616 BIOSIS

DN PREV200000418616
TI Molecular cloning and functional characterization of murine Transmembrane Activator and CAML Interactor (TACI) with chromosomal localization in human and mouse.
AU von Bulow, Gotz-Ulrich; Russell, Helen; Copeland, Neal G.; Gilbert, Debra J.; Jenkins, Nancy A.; Bram, Richard J. (1)
CS (1) Department of Pediatrics and Adolescent Medicine, Mayo Foundation, 200 1st Street SW, Rochester, MN, 55905 USA
SO Mammalian Genome, (August, 2000) Vol. 11, No. 8, pp. 628-632. print. ISSN: 0938-8990.
DT Article
LA English
SL English
AB The human Taci gene (Transmembrane Activator and CAML Interactor) encodes a recently discovered member of the Tumor Necrosis Factor Receptor family. TACI is expressed in B-lymphocytes and may act to regulate humoral immunity. To identify functionally important regions of the protein, we have isolated and characterized the murine homolog of the human Taci cDNA. The proteins display 61.5% similarity and 54.6% identity. Mouse TACI is a type III transmembrane protein, as judged by the lack of a cleaved signal sequence and its N-terminal extracellular exposure. The intracellular domains of the mouse and human proteins share a single, defined region of high sequence conservation (19 of 23 residues identical). This constitutes a novel domain that may play a part in the initiation of signal transduction through TACI. In support of this notion, mouse TACI was found to activate NFAT, ***NFkB*** , and AP1 transcription factors in a transient transfection assay. The Taci gene was localized to human Chromosome (Chr) 17p11 by fluorescence in situ hybridization. The murine homolog was localized by intraspecific backcross analysis to the middle of Chr 11, a region that is syntenic to human Chr 17p. This work identifies conserved domains within TACI that may mediate the cellular distribution and signal transduction function of the protein and extend the details of homology between mouse Chr 11 and human 17p.

L17 ANSWER 16 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3
AN 2000:279667 BIOSIS
DN PREV200000279667
TI The Epstein-Barr virus latent membrane protein 1 (LMP1) enhances TNF alpha-induced apoptosis of intestine 407 epithelial cells: The role of LMP1 C-terminal activation regions 1 and 2.
AU Kawanishi, Michiko (1)
CS (1) Department of Microbiology, Graduate School of Medicine, Kyoto University, Kyoto, 606-8315 Japan
SO Virology, (May 10, 2000) Vol. 270, No. 2, pp. 258-266. print. ISSN: 0042-6822.
DT Article
LA English
SL English
AB Epstein-Barr virus (EBV) latent membrane protein 1 (LMP1) can protect some kinds of lymphocytes from apoptotic cell death. In contrast, the present study showed that the expression of LMP1 induced high susceptibility to tumor necrosis factor alpha (TNFalpha)-induced apoptosis in intestine 407 epithelial cells, without affecting expression of ***TNF*** ***receptors*** I and II. LMP1-deletion mutants lacking either C-terminal activation region (CTAR)-1 or CTAR-2 had ability to enhance TNFalpha-induced apoptosis, whereas the deletion of both activation regions completely abolished the induction of high susceptibility to TNFalpha. Phosphorylation of the ***NFkB*** -inhibitory molecule IkB-alpha, another biological activity of TNFalpha, was not enhanced by LMP1-expression. LMP1 upregulated antiapoptotic gene A20 expression, suggesting that A20 can not block TNFalpha-induced apoptosis in this cell system. Apoptosis triggered by TNFalpha in LMP1-expressing intestine 407 cells was blocked by inhibitors of caspases-8 and -3. It is therefore concluded that in intestine 407 epithelial cells, LMP1 enhances primarily signal cascade responsible for TNFalpha-induced apoptosis, which occurs at a level upstream of acting site of caspases-8 and -3 and that CTAR-1 and CTAR-2 are involved in enhancement of TNFalpha-induced apoptosis.

L17 ANSWER 17 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:311537 BIOSIS
DN PREV200100311537
TI SDF-1 activity regulation by CD30 cross-linking in the CD4+/CD30+ cell line L540.
AU Vinante, Fabrizio (1); Rigo, Antonella (1); Pizzolo, Giovanni (1)
CS (1) Department of Clinical and Experimental Medicine, Section of Hematology, University of Verona, Verona Italy
SO Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 241a. print. Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology . ISSN: 0006-4971.
DT Conference
LA English
SL English
AB The so far elucidated activities induced after stimulation of CD30 (a ***TNF*** -family ***receptor*** up-regulated by IL-4 and preferentially expressed/released by persistently activated Th2/0 lymphocytes) seem to integrate chemokine-driven modulation of cellular functions. Thus, we evaluated the possibility that signals transduced through CD30 may regulate some chemokines and/or chemokine receptors. To this purpose, we used the CD4+/CD30+ cell line L540, which is an established model to study CD30-mediated activation. L540 cells expressed costitutively on their membrane the SDF-1 receptor CXCR4 (MFI at flow cytometry: range 101-120; mAb from Pharmingen) and released low amounts of MIP-1 alpha (range 20-41 pg/mL) and RANTES (0.3-80 pg/mL) (Amersham ELISA kit) in standard culture conditions, while PMA stimulation induced high amounts of both chemokines. Agonistic anti-CD30 mAbs (M44 and M67, Immunex) induced nuclear mobilization of p50/p65 ***NFkB*** as well as AP-1 in supershift assays. At 48 hours, a down-regulation of membrane CD30 (p=0.008) was observed which correlated with increased sCD30 concentration in culture supernatants (mean+-SEM: basal 19.3+-5.5 vs stimulated 99.8+-12 U/mL, p=0.0006; DAKO ELISA kit). By contrast, membrane CXCR4 was up-regulated, followed by an enhancement of the chemotactic activity exerted by SDF-1 on L540 cells. This CD30-mediated effect was associated with a decrease in the rate of cell proliferation. Moreover, it was associated with no or little effect on the production of RANTES (lower than 3 pg/mL) and with an apparent inhibitory effect on the release of MIP-1 alpha (mean+-SEM: basal 33.9+-9vs stimulated 10.8+-2.3 pg/mL, p=0.026), though RPA showed a faint, early induction of MIP-1 alpha mRNA. Thus, CD30 cross-linking can lead to a modulation of CXCR4 and MIP-1 alpha expression in L540 cells modifying their sensitivity to SDF-1. This suggests that CD30-related pathways are involved in chemokine-driven activities possibly in the context of T cell priming mechanisms.

L17 ANSWER 18 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:289121 BIOSIS
DN PREV200100289121
TI Distinct signals induced by VEGF and ***TNF*** ***receptors*** converge at MEK and lead to EGR-1 and tissue factor (TF) upregulation in endothelial cells.
AU Mechtcheriakova, Diana (1); Schabbauer, Gernot (1); Lucerna, Markus (1); Binder, Bernd R. (1); Hofer, Erhard (1)
CS (1) Vascular Biology, University of Vienna, Vienna Austria
SO Blood, (November 16, 2000) Vol. 96, No. 11 Part 2, pp. 140b. print. Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology . ISSN: 0006-4971.
DT Conference
LA English
SL English
AB TF has been shown to be upregulated in endothelial cells not only by inflammatory cytokines such as TNF-a but also by VEGF, supporting a potential role of TFfor angiogenesis (Mechtcheriakova et al., Blood 1999; 93; 3811). Since both stimuli induce the transcription factor EGR-1, which is critically involved in TF gene regulation, we used EGR-1 dependent TF induction as a model to identify potential cross-talk between specific signal transduction cascades initiated by VEGF and TNF. The obtained data show that VEGF mainly activates the MEK/ERK and p38 MAP kinases, whereas TNF is able to strongly activate all three major MAP kinase (MEK/ERK, p38, JNK) and the ***NFkB*** pathways. The MEK/ERK MAP kinase module appears to act as convergence point of distinct upstream VEGF and TNF-initiated signal cascades leading to TF induction via EGR-1. The VEGF signaling is characterized by a strong PKC-dependence, whereas the TNF signals can be selectively blocked by a mutant of IkB kinase-2. The involvement of PKC in VEGF signaling is a specific property of this factor, since e.g. EGF induction of MEK/ERK is independent of PKC and this is not sufficient to upregulate TF. Furthermore, it is possible that also a second factor(s) is important for the full response of the TF promoter. NFAT could be one of the candidates, since NFAT has been shown to be activated by VEGF. In line with an important role of EGR-1, the corepressor NAB2 can block VEGF-induced TF transcription. In summary, our data suggest i) a new link between the inflammatory ***NFkB*** and the MEK/ERK MAP kinase cascades, ii) a specificity of VEGF signals in comparison to other growth factors and iii) the potential use of NAB2 to inhibit VEGF/EGR-1-dependent genes.

L17 ANSWER 19 OF 30 CAPLUS COPYRIGHT 2002 ACS
AN 1999:570982 CAPLUS
DN 131:284510
TI NF-.kappa.B induces expression of the Bcl-2 homologue A1/Bfl-1 to preferentially suppress chemotherapy-induced apoptosis
AU Wang, Cun-Yu; Guttridge, Denis C.; Mayo, Marty W.; Baldwin, Albert S., Jr.
CS Laboratory of Molecular Signaling and Apoptotsis, School of Dentistry, University of North Carolina, Chapel Hill, NY, 27599, USA
SO Molecular and Cellular Biology (1999), 19(9), 5923-5929 CODEN: MCEBD4; ISSN: 0270-7306
PB American Society for Microbiology
DT Journal
LA English
AB Recent evidence indicates that the transcription factor NF-.kappa.B is a major effector of inducible antiapoptotic mechanisms. For example, it was shown that NF-.kappa.B activation suppresses the activation of caspase 8, the apical caspase in tumor necrosis factor (***TNF***) ***receptor*** family signaling cascades, through the transcriptional regulation of certain TRAF and IAP proteins. However, it was unknown whether NF-.kappa.B controls other key regulatory mechanisms in apoptosis. Here we show that NF-.kappa.B activation suppresses mitochondrial release of cytochrome c through the activation of the Bcl-2 family member A1/Bfl-1. The restoration of A1 in NF-.kappa.B null cells diminished

TNF-induced apoptosis by reducing the release of proapoptotic cytochrome c from mitochondria. In addn., A1 potently inhibited etoposide-induced apoptosis by inhibiting the release of cytochrome c and by blocking caspase 3 activation. Our findings demonstrate that A1 is an important antiapoptotic gene controlled by NF-.kappa.B and establish that the prosurvival function of NF-.kappa.B can be manifested at multiple levels.
RE.CNT 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 20 OF 30 CAPLUS COPYRIGHT 2002 ACS
AN 1999:602627 CAPLUS
DN 132:31443
TI ECSIT is an evolutionarily conserved intermediate in the Toll/IL-1 signal transduction pathway
AU Kopp, Elizabeth; Medzhitov, Ruslan; Carothers, James; Xiao, Changchun; Douglas, Iris; Janeway, Charles A.; Ghosh, Sankar
CS Section of Immunobiology and Department of Molecular Biophysics and Biochemistry, Howard Hughes Medical Institute (HHMI), Yale University School of Medicine, New Haven, CT, 06520, USA
SO Genes & Development (1999), 13(16), 2059-2071
CODEN: GEDEEP; ISSN: 0890-9369
PB Cold Spring Harbor Laboratory Press
DT Journal
LA English
AB Activation of NF-.kappa.B as a consequence of signaling through the Toll and IL-1 receptors is a major element of innate immune responses. We report the identification and characterization of a novel intermediate in these signaling pathways that bridges TRAF6 to MEKK-1. This adapter protein, which we have named ECSIT (evolutionarily conserved signaling intermediate in Toll pathways), is specific for the Toll/IL-1 pathways and is a regulator of MEKK-1 processing. Expression of wild-type ECSIT accelerates processing of MEKK-1, whereas a dominant-neg. fragment of ECSIT blocks MEKK-1 processing and activation of NF-.kappa.B. These results indicate an important role for ECSIT in signaling to NF-.kappa.B and suggest that processing of MEKK-1 is required for its function in the Toll/IL-1 pathway.
RE.CNT 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 21 OF 30 CAPLUS COPYRIGHT 2002 ACS
AN 1999:414305 CAPLUS
DN 131:209943
TI The zinc finger protein A20 inhibits TNF-induced NF-.kappa.B-dependent gene expression by interfering with an RIP- or TRAF2-mediated transactivation signal and directly binds to a novel NF-.kappa.B-inhibiting protein ABIN
AU Heyninck, Karen; De Valck, Dirk; Vanden Berghe, Wim; Van Criekinge, Wim; Contreras, Roland; Fiers, Walter; Haegeman, Guy; Beyaert, Rudi
CS Department of Molecular Biology, Flanders Interuniversity Institute for Biotechnology, University of Ghent, Ghent, B-9000, Belg.
SO Journal of Cell Biology (1999), 145(7), 1471-1482
CODEN: JCLBA3; ISSN: 0021-9525
PB Rockefeller University Press
DT Journal
LA English
AB The zinc finger protein A20 is a tumor necrosis factor (TNF)- and interleukin 1 (IL-1)-inducible protein that neg. regulates nuclear factor-kappa B (NF-.kappa.B)-dependent gene expression. However, the mol. mechanism by which A20 exerts this effect is still unclear. We show that A20 does not inhibit TNF-induced nuclear translocation and DNA binding of NF-.kappa.B, although it completely prevents the TNF-induced activation of an NF-.kappa.B-dependent reporter gene, as well as TNF-induced IL-6 and granulocyte macrophage-colony stimulating factor gene expression. Moreover, NF-.kappa.B activation induced by overexpression of the ***TNF*** ***receptor*** -assocd. proteins ***TNF*** ***receptor*** -assocd. death domain protein (TRADD), receptor interacting protein (RIP), and ***TNF*** ***receptor*** -assocd. factor 2 (TRAF2) was also inhibited by expression of A20, whereas NF-.kappa.B activation induced by overexpression of NF-.kappa.B-inducing kinase (NIK) or the human T cell leukemia virus type 1 (HTLV-1) Tax was unaffected. These results demonstrate that A20 inhibits NF-.kappa.B-dependent gene expression by interfering with a novel TNF-induced and RIP- or TRAF2-mediated pathway that is different from the NIK-I.kappa.B kinase pathway and that is specifically involved in the transactivation of NF-.kappa.B. Via yeast two-hybrid screening, we found that A20 binds to a novel protein, ABIN, which mimics the NF-.kappa.B inhibiting effects of A20 upon overexpression, suggesting that the effect of A20 is mediated by its interaction with this NF-.kappa.B inhibiting protein, ABIN.
RE.CNT 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 22 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:46913 BIOSIS
DN PREV200000046913
TI Arsenic compounds induce apoptosis in multiple myeloma (MM): Role of ***NFKb*** -RIP pathway.
AU Pearse, R. (1); Bajenova, O. (1); Feinman, R. (1); Tang, B. (1); Childs, B. (1); Michaeli, J. (1)
CS (1) Memorial Sloan-Kettering Cancer Center, New York, NY USA
SO Blood, (Nov. 15, 1999) Vol. 94, No. 10 SUPPL. 1 PART 1, pp. 309a.
Meeting Info.: Forty-first Annual Meeting of the American Society of Hematology New Orleans, Louisiana, USA December 3-7, 1999 The American Society of Hematology
. ISSN: 0006-4971.
DT Conference
LA English

L17 ANSWER 23 OF 30 CAPLUS COPYRIGHT 2002 ACS
AN 2000:18895 CAPLUS
DN 132:205908
TI Induction of negative regulators of haematopoiesis in human bone marrow cells by HLA-DR cross-linking
AU Yamaguchi, Masaki; Nadler, Steve; Lee, Jong-Wook; Deeg, H. Joachim
CS Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA, 98109, USA
SO Transplant Immunology (1999), 7(3), 159-168
CODEN: TRIME2; ISSN: 0966-3274
PB Arnold, Hodder Headline
DT Journal
LA English
AB Tumor necrosis factor-alpha (TNF.alpha.) is up-regulated by crosslinking of major histocompatibility complex (MHC) class II [human leukocyte antigen (HLA)-DR] antigens on monocytes. This is done by a bacterial superantigen or anti-HLA-DR monoclonal antibody (MAb). We have previously shown that HLA-DR crosslinking results in inhibition of haematopoiesis and apoptosis. TNF.alpha. acts as a neg. regulator of haematopoiesis. Here we investigated whether HLA-DR-mediated inhibition of haematopoiesis involved TNF.alpha. and TNF.alpha.-dependent secondary signals. Anti-HLA-DR MAb H81.9 up-regulated TNF.alpha., as well as transforming growth factor .beta., interleukin (IL)-1.beta. and IL-6 in human marrow cells at the RNA (RNA) and protein level. The effect on TNF.alpha. was investigated further. Up-regulation was blocked by herbimycin A, consistent with a tyrosine kinase-dependent mechanism. Up-regulation was also blunted by the sol. ***TNF*** - ***receptor*** fusion protein TNFR:Fc, suggesting an autocrine amplification loop. Following TNF.alpha. up-regulation, there was increased expression of Fas (CD95) and Fas-ligand (Fas-L). Up-regulation of Fas and Fas-L was blocked by TNFR:Fc. Furthermore, MAb H81.9-induced apoptosis was prevented by anti-TNF.alpha. MAb and by the sol. Fas receptor, Fas-Ig, providing further evidence that the TNF effect was mediated via Fas. At the transcriptional level, crosslinking of HLA-DR by MAb H81.9 affects nuclear localization of ***NFkB*** , which is involved in the transcription of TNF.alpha.. ***NFkB*** activity is modified by changes in cellular redox potential, and we have shown that H81.9 affects redox potential as detd. by the generation of nitric oxide. These data show that HLA-DR-initiated signals are able to trigger a cascade of neg. regulators of haematopoiesis. This model provides an opportunity to dissect signalling pathways that may be involved in the development of spontaneous marrow failure, and to devise interventions aimed at protecting haematopoiesis.
RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 24 OF 30 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 4
AN 1998397057 EMBASE
TI Nuclear factor kB-independent cytoprotective pathways originating at tumor necrosis factor receptor-associated factor 2.
AU Natoli G.; Costanzo A.; Guido F.; Moretti F.; Bernardo A.; Burgio V.L.; Agresti C.; Levrero M.
CS M. Levrero, Fondazione Andrea Cesalpino, Policlinico Umberto I, University of Rome La Sapienza, Viale del Policlinico 155, 00161 Rome, Italy. levmax@mix.it
SO Journal of Biological Chemistry, (20 Nov 1998) 273/47 (31262-31272).
Refs: 69
ISSN: 0021-9258 CODEN: JBCHA3
CY United States
DT Journal; Article
FS 029 Clinical Biochemistry
LA English
SL English
AB Most normal and neoplastic cell types are resistant to tumor necrosis factor (TNF) cytotoxicity unless cotreated with protein or RNA synthesis inhibitors, such as cycloheximide and actinomycin D. Cellular resistance to ***TNF*** requires ***TNF*** ***receptor*** -associated factor 2 (TRAF2), which has been hypothesized to act mainly by mediating activation of the transcription factors nuclear factor kB (***NFkB***) and activator protein 1 (AP1). ***NFkB*** was proposed to switch on transcription of yet unidentified anti-apoptotic genes. To test the possible existence of ***NFkB*** -independent cytoprotective pathways, we systematically compared selective trans-dominant inhibitors of the ***NFkB*** pathway with inhibitors of TRAF2 signaling for their effect on TNF cytotoxicity. Blockade of TRAF2 function(s) by signaling-deficient oligomerization partners or by molecules affecting TRAF2 recruitment to the ***TNF*** ***receptor*** 1 complex completely abrogated the cytoprotective response. Conversely, sensitization to TNF cytotoxicity induced by a selective ***NFkB*** blockade affected only a fraction of TNF-treated cells in an apparently stochastic manner. No cytoprotective role for c-Jun amino-terminal kinases/stress-activated protein kinases (JNKs/SAPKs), which are activated by TRAF2 and contribute to stimulation of activator protein 1 activity, could be demonstrated in the cellular

systems tested. Although required for cytoprotection, TRAF2 is not sufficient to protect cells from TNF + cycloheximide cytotoxicity when overexpressed in transfected cells, thus indicating an essential role of additional ***TNF*** ***receptor*** 1 complex components in the cytoprotective response. Our results indicate that TNF-induced cytoprotection is a complex function requiring the integration of multiple signal transduction pathways.

L17 ANSWER 25 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1998:228293 BIOSIS
DN PREV199800228293
TI hUBC9 associates with MEKK1 and type I ***TNF*** -alpha ***receptor*** and stimulates NFkappaB activity.
AU Saltzman, Alan; Searfoss, George; Marcireau, Christophe; Stone, Maureen; Ressner, Rose; Munro, Robin; Franks, Carol; D'Alonzo, Jill; Tocque, Bruno; Jaye, Michael; Ivashchenko, Yuri (1)
CS (1) Rhone-Poulenc River Central Res., Gene Med. Dep., 500 Arcola Rd., Collegeville, PA 19426 USA
SO FEBS Letters, (April 3, 1998) Vol. 425, No. 3, pp. 431-435. ISSN: 0014-5793.
DT Article
LA English
AB hUBC9, an E2 ubiquitin conjugating enzyme, was identified by yeast two-hybrid screening and coprecipitation studies to interact with MEKK1 and the type I ***TNF*** -alpha ***receptor*** , respectively. Because both of these proteins regulate ***NFKB*** activity, the role of hUBC9 in modulating NFkappaB activity was investigated. Overexpression of hUBC9 in HeLa cells stimulated the activity of NFkappaB as determined by NFkappaB reporter and IL-6 secretion assays. hUBC9 also synergized with MEKK1 to activate NFkappaB reporter activity. Thus, hUBC9 modulates NFkappaB activity which, at least in part, can be attributed to its interaction with MEKK1 and the type I ***TNF*** -alpha ***receptor*** .

L17 ANSWER 26 OF 30 CAPLUS COPYRIGHT 2002 ACS
AN 1997:740095 CAPLUS
DN 127:355669
TI Method of enhancing the effect of neurotrophin with analogs of p75NTR367-379
IN Riopelle, Richard J.; Weaver, Donald F.; Ross, Gregory M.; Shamovsky, Igor L.
PA Shamovsky, Igor L., Can.; Queen's University At Kingston; Riopelle, Richard J.; Weaver, Donald F.; Ross, Gregory M.
SO PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9740809	A2	19971106	WO 1997-CA271	19970423
WO 9740809	A3	19980326		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2252469	AA	19971106	CA 1997-2252469	19970423
AU 9725634	A1	19971119	AU 1997-25634	19970423
US 6417159	B1	20020709	US 1997-839131	19970423
PRAI GB 1996-8335	A	19960423		
WO 1997-CA271	W	19970423		

AB The present invention provides methods and compns. for enhancing an effect or effects of a neurotrophin, preferably, but not limited to, enhancing the growth and survival promoting properties of neurotrophins. The cytoplasmic region of the common neurotrophin receptor (p75NTR) (rat, human, chick) contains a putative membrane-assocg. domain implicated in intracellular signaling. A peptide (R3) identical to this domain (p75NTR367-379) and various analogs of this peptide displayed CD spectra in aq. and non-polar environments identical to the amphiphilic tetradecapeptide mastoparan (MP), and were internalized by PC12 rat pheochromocytoma cells. The R3 peptide enhanced neurite growth in PC12 cells, chick embryo primary sensory neurons, and fetal rat primary sensory neurons in vitro in the presence of sub-satg. concns. of NGF. Peptide analogs of R3 not faithful to the distance and angular relationships of ionic groups, and the putative amphiphilic structure of p75NTR367-379, while still providing some enhancement, nevertheless displayed reduced potency to enhance NGF-mediated neurite growth. The common neurotrophin receptor p75NTR activates and translocates the nuclear transcription factor ***NFkB*** and displays pro-apoptotic effects similar to other members of the ***TNF*** ***receptor*** superfamily. A peptide mimic of the amphiphilic domain 367-379 of p75NTR that enhances TrkA mediated neurite growth by NGF, was used to affinity purify cytoplasmic proteins from PC12 cells. Isolated proteins contained a predominant species with an apparent mol. wt. of 65 kDa. The affinity purified 65 kDa protein, as well as a protein of similar mol. mass from crude cell exts., were identified by immunoblotting with antibody to NF.kappa.B. The 65 kDa species was chem. cross-linked to the radiolabeled analog of the peptide mimic of p75NTR and immunopptd. by antibody to ***NFkB*** . These observations, taken together with the finding that a p75NTR-selective NGF antagonist blocked mediated neurite growth in limiting NGF conditions, support the view that p75NTR participates in neurite growth via a signaling pathway involving the translocation of NF.kappa.B.

L17 ANSWER 27 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1996:123955 BIOSIS
DN PREV199698696090
TI Apoptosis mediated by the ***TNF*** -related cytokine and ***receptor*** families.
AU Ware, Carl F. (1); Vanarsdale, Sammee; Vanarsdale, Todd L.
CS (1) Div. Biomedical Sci., Univ. California, Riverside, CA 92521 USA
SO Journal of Cellular Biochemistry, (1996) Vol. 60, No. 1, pp. 47-55. ISSN: 0730-2312.
DT General Review
LA English
AB T lymphocytes use several specialized mechanisms to induce apoptotic cell death. The tumor necrosis factor (TNF)-related family of membrane-anchored and secreted ligands represent a major mechanism regulating cell death and cell survival. These ligands also coordinate differentiation of tissue to defend against intracellular pathogens and regulate development of lymphoid tissue. Cellular responses are initiated by a corresponding family of specific receptors that includes two distinct TNFR (TNFR60 and TNFR80), Fas (CD95), CD40, p75NTF, and the recently identified lymphotoxin beta-receptor (LT-beta-R), among others. The MHC-encoded cytokines, TNF and LT-alpha, form homomeric trimers, whereas LT-beta assembles into heterotrimers with LT-alpha, creating multimeric ligands with distinct receptor specificities. The signal transduction cascade is initiated by transmembrane aggregation (clustering) of receptor cytoplasmic domains induced by binding to their multivalent ligands. The TRAF family of Zn RING/finger proteins bind to TNFR80; CD40 and LT-beta-R are involved in induction ***NFKB*** and cell survival. TNFR60 and Fas interact with several distinct cytosolic proteins sharing the "death domain" homology region. TNF binding to TNFR60 activates a serine protein kinase activity and phosphoproteins are recruited to the receptor forming a multicomponent signaling complex. Thus, TNFRs use diverse sets of signaling molecules to initiate and regulate cell death and survival pathways.

L17 ANSWER 28 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 5
AN 1994:449642 BIOSIS
DN PREV199497462642
TI Acid sphingomyelinase is not essential for the IL-1 and tumor necrosis factor receptor signaling pathway leading to ***NFkB*** activation.
AU Kuno, Kouji; Sukegawa, Kazuko; Ishikawa, Yuji; Orii, Tadao; Matsushima, Kouji (1)
CS (1) Dep. Pharmacol., Cancer Res. Inst., Kanazawa Univ., Takara-Machi 13-1, Kanazawa 920 Japan
SO International Immunology, (1994) Vol. 6, No. 8, pp. 1269-1272. ISSN: 0953-8178.
DT Article
LA English
AB A recent report has suggested that tumor necrosis factor (TNF) utilizes acid sphingomyelinase (SMase) pathway to activate ***NFkB*** (Schulze et al. 1992. Cell 71:765). To directly investigate the role of acid SMase in IL-1 and ***TNF*** ***receptor*** -mediated signal transduction, we examined the ability of Niemann-Pick disease (NPD) type A fibroblasts, which are deficient in acid SMase, to induce IL-8 gene expression through activating ***NFkB*** . Unexpectedly, IL-1-alpha and TNF-alpha efficiently induced IL-8 production and IL-8 mRNA in NPD type A fibroblasts as in normal fibroblasts. Furthermore, activation of ***NFkB*** was also induced in NPD type A fibroblasts in response to IL-1-alpha and TNF-alpha stimulation to a similar extent as in normal fibroblasts. These results provide evidence that acid SMase is not essential in IL-1 and ***TNF*** ***receptor*** signaling leading to ***NFkB*** activation as well as the cytokine gene activation which is regulated by ***NFkB*** .

L17 ANSWER 29 OF 30 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 92156130 EMBASE
DN 1992156130
TI Mechanisms of tumor necrosis factor action.
AU Schutze S.; Machleidt T.; Kronke M.
CS Inst. fur Med. Mikrobiologie/Hygiene, Technische Universitat Munchen, Trogerstr. 4a,8000 Munchen 80, Germany
SO Seminars in Oncology, (1992) 19/2 SUPPL. 4 (16-24). ISSN: 0093-7754 CODEN: SOLGAV
CY United States
DT Journal; Conference Article
FS 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LA English
SL English
AB Tumor necrosis factor (TNF) is able to induce a great diversity of cellular responses via modulating the expression of a number of different genes. The multitude of TNF activities may be explained by both structural and functional heterogeneity in ***TNF*** ***receptors*** as well as by a diversification of postreceptor signal transduction pathways. Purification of ***TNF*** ***receptors*** has revealed two major, distinct binding proteins (TR60 and TR80). TR60 seems to be an essential component for TNF signaling; the functional role of TR80 remains to be

elucidated. The pathway of postreceptor signal transduction involves phospholipase A2, a phosphatidylcholine-specific phospholipase C, protein kinase C, and other serine/threonine and tyrosine-specific protein kinases with as yet unknown function. At the receiving end of TNF signaling, induction of gene expression is mediated through activation of nuclear transcription factors, such as ***NFkB*** , AP-1, IRF-1, and NF-GMa.

L17 ANSWER 30 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1991:38574 BIOSIS
DN BR40:15554
TI TNF INDUCED ***NFKB*** -HIV-1-LTR ACTIVATION CAN BE EFFICIENTLY BLOCKED
BY AN ANTI- ***TNF*** - ***RECEPTOR*** P60 ANTIBODY.
AU KRUPPA G; MEICHLE A; THOMA B; SCHEURICH P; PFIZENMAIER K; KROENKE M
CS CLINICAL RES. GROUP, MAX-PLANCK SOCIETY, GOSSLERSTR. 10D, 3400 GOETTINGEN,
FRG.
SO SEVENTH INTERNATIONAL LYMPHOKINE WORKSHOP, SAN ANTONIO, TEXAS, USA,
OCTOBER 1-5, 1990. LYMPHOKINE RES. (1990) 9 (4), 573.
CODEN: LYREDH. ISSN: 0277-6766.
DT Conference
FS BR; OLD
LA English

=> d his

(FILE 'HOME' ENTERED AT 14:56:09 ON 06 NOV 2002)

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 14:56:17 ON 06 NOV 2002
L1 1 S TNF RECEPTOR ASSOCIATED WITH DEATH PROTEIN? OR TNF RECEPTOR A
L2 3 S TRADE ALPHA OR TRADE BETA
L3 3 DUP REM L2 (0 DUPLICATES REMOVED)
L4 599 S TNF RECEPTOR FAMIL?
L5 2 S L4 AND TRADE
L6 2 DUP REM L5 (0 DUPLICATES REMOVED)
L7 0 S L6 NOT L3
L8 2 S OAF065
L9 2 DUP REM L8 (0 DUPLICATES REMOVED)
L10 12584 S TNF (3A) RECEPTOR?
L11 973 S L10 AND REVIEW

FILE 'STNGUIDE' ENTERED AT 15:17:48 ON 06 NOV 2002

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 15:22:21 ON 06 NOV 2002
L12 3 S L10 AND TRADE
L13 3 DUP REM L12 (0 DUPLICATES REMOVED)
L14 187 S L11 AND (CELL PROLIFER? OR CELL DEATH)
L15 134 DUP REM L14 (53 DUPLICATES REMOVED)
L16 36 S L10 AND NFKB
L17 30 DUP REM L16 (6 DUPLICATES REMOVED)

=> d bib abs l15 1-10

L15 ANSWER 1 OF 134 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 2002345093 EMBASE
TI BAFF et al.: Novel members of the ***TNF*** ligand and ***receptor*** families as therapeutic targets.
AU Dumont F.J.
CS F.J. Dumont, Merck Research Laboratories, 126 Lincoln Avenue, Rahway, NJ 07065, United States. francisdumont@merck.com
SO Expert Opinion on Therapeutic Patents, (2002) 12/9 (1351-1365).
Refs: 98
ISSN: 1354-3776 CODEN: EOTPEG
CY United Kingdom
DT Journal; General Review
FS 022 Human Genetics
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
039 Pharmacy
LA English
SL English
AB Tumour necrosis factor (TNF) family ligands and their corresponding receptors play important roles in the immune system, where they regulate lymphoid organ development and influence immune ***cell*** ***proliferation*** , differentiation, activation and death. Several TNF family members, including TNF-.alpha. and CD154, have already provided valuable therapeutic targets for the treatment of immune-mediated diseases. Over the past three years, a new subfamily of ***TNF*** -related ligands/ ***receptors*** , which also plays a role in immunity, has been discovered by sequence-homology database searches. This subfamily, which appears to be particularly important in B cell immunity, includes two ligands termed B cell activating factor of the TNF family (BAFF) and a proliferation-inducing ligand (APRIL) and at least three receptors: B cell maturation protein (BCMA) and transmembrane activator and calcium modulator and cyclophilin ligand interactor (TACI), which bind both ligands, and BAFF receptor (BAFF-R), which binds only BAFF. Besides promoting the survival of B cells and regulating their proliferation and differentiation in collaboration with signals from the B cell antigen receptor, BAFF and APRIL may modulate T cell activation and APRIL may also act as an autocrine growth factor for certain tumour cells. There is evidence that overproduction of BAFF in mice results in a B cell-mediated autoimmune syndrome resembling systemic lupus erythematosus (SLE), and that elevated levels of this cytokine are associated with SLE and rheumatoid arthritis in humans. The discovery of this novel ligand/receptor network has provided novel insights into the mechanisms of immunoregulation. Most importantly, it offers the opportunity for developing novel treatment strategies for autoimmune diseases, immunodeficiencies, lymphoma and cancer. The prospect of exploiting this new information for therapeutic purposes has generated a flurry of recent patent applications that are discussed here.

L15 ANSWER 2 OF 134 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 2002318202 EMBASE
TI [Alteration of ***cell*** ***death*** -related genes in human diseases].
IMPLICATIONS PHYSIOPATHOLOGIQUES DES ALTERATIONS DES GENES IMPLIQUES DANS
LA REGULATION DE LA MORT CELLULAIRE.
AU Solary E.; Bettaieb A.; Dubrez-Daloz L.; Garrido C.
CS E. Solary, Inserm U.517, IFR 100, UFR de Medecine/Pharmacie, 7, boulevard Jeanne d'Arc, 21000 Dijon, France. esolary@u-bourgogne.fr
SO Medecine/Sciences, (2002) 18/8-9 (861-873).
Refs: 51
ISSN: 0767-0974 CODEN: MSMSE4
CY France
DT Journal; General Review
FS 022 Human Genetics
029 Clinical Biochemistry
LA French
SL English; French
AB ***Cell*** ***death*** by apoptosis is a fundamental process that regulates tissue development and homeostasis. Deregulation of this process is involved in a number of human diseases and this deregulation can be related to inherited or acquired genetic abnormalities of proteins involved in the death machinery. Most inherited mutations interfere with the death receptor signalling pathways, including Fas, Fas-ligand or caspase-10 mutations in the Canale-Smith syndrome, deletion of NEMO (IKK.gamma.) gene in familial incontinentia pigmenti and mutations in the extracellular domains of the 55 kDa ***TNF*** ***receptor*** in a dominant autoinflammatory syndrome. Familial Mediterranean fever was related to mutations in the MEFV gene whose product interacts with the pro-apoptotic protein ASC. Perforin gene defects were identified in familial hemophagocytic lymphohistiocytosis whereas alterations of naip gene, that encodes a caspase inhibitory protein, increase the severity of spinal amyotrophy. In human tumors, three mechanisms were observed to account for acquired ***cell*** ***death*** gene alteration: chromosomal translocation leading to overexpression of a normal (Bcl-2) or mutated (Bcl-10, c-IAP2) protein, gene mutation leading to functional alterations of the protein (p53, Fas, Box) and gene promoter hypermethylation that prevents the protein expression (caspase 8, Apaf-1, DAP kinase, TMS1). Depending on the disease, these genetic abnormalities can now be used as diagnostic tools, prognostic markers and therapeutic targets.

L15 ANSWER 3 OF 134 CAPLUS COPYRIGHT 2002 ACS
AN 2002:224463 CAPLUS
DN 137:18893
TI ***TNF*** ligands and ***receptors*** - a matter of life and death
AU MacEwan, David J.
CS Department of Biomedical Sciences, Institute of Medical Sciences, University of Aberdeen, Aberdeen, AB25 2ZD, UK
SO British Journal of Pharmacology (2002), 135(4), 855-875
CODEN: BJPCBM; ISSN: 0007-1188
PB Nature Publishing Group
DT Journal; General Review
LA English
AB A ***review*** . This paper focuses on the mol. aspects and biol. role of tumor necrosis factor (TNF). Topics discussed include ***TNF*** ***receptor*** (TNFR) signaling mechanisms; lipase activities; kinases and phosphatases; the role of caspase in apoptotic ***cell*** ***death*** ; role of G-proteins and Ca2+ in TNFR signaling; physiol. role of TNFR; and the therapeutic implications of ***TNF*** ligands and ***receptors*** .
RE.CNT 317 THERE ARE 317 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 134 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 2002318200 EMBASE
TI [Programmed ***cell*** ***death*** ' regulation: Towards a more dynamic conception].
REGULATION DE LA MORT CELLULAIRE PROGRAMMEE: VERS UNE CONCEPTION PLUS
DYNAMIQUE.
AU Couzinet A.; Herincs Z.; Hueber A.-O.
CS A.-O. Hueber, Institut Biol. du Development/Cancer, Cnrs UMR 6543, Centre Antoine Lacassagne, 33, avenue de Valombrose, 06189 Nice Cedex 2, France. hueber@unice.fr
SO Medecine/Sciences, (2002) 18/8-9 (841-852).
Refs: 49

ISSN: 0767-0974 CODEN: MSMSE4
CY France
DT Journal; General Review
FS 029 Clinical Biochemistry
LA French
SL English; French
AB Programmed ***cell*** ***death*** is essential for the development and maintenance of multicellular organisms and alterations in control of ***cell*** ***death*** /survival contribute to the pathogenesis of many human diseases. ***Cell*** ***death*** is ultimately executed by caspases, a family of cysteinil aspartate specific proteinases that cleave critical intracellular proteins and execute the apoptotic program. At least two major pathways for caspase activation have been identified: (1) the receptor-mediated pathway which involves members of the tumor necrosis factor (***TNF***) family of death ***receptors*** and (2) the mitochondrial-mediated pathway involving SIMP (soluble inter membrane mitochondrial proteins) released from the mitochondria. A formation of a multi protein complex which forms a template for efficient caspase processing is characteristic for each pathway respectively: the DISC (death inducing signaling complex) is formed by the death receptor and a set of cytosolic adaptor proteins (including procaspase) rapidly recruited to the membrane after ligand binding, and the apoptosome contains cytochrome c, Apaf-1 and procaspase 9. The function of these two complexes is modified at different levels by multiple inhibitory proteins: Flips (FADD-like ICE inhibitory proteins), IAPs (inhibitor of apoptosis protein) and the Bcl-2 family members. The role of other protein complexes formed at other locations within the cell, such as the nucleus that might have a role in ***cell*** ***death*** regulation will be also discussed.

L15 ANSWER 5 OF 134 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
1
AN 2002:268294 BIOSIS
DN PREV200200268294
TI ***TNF*** ***receptor*** subtype signalling: Differences and cellular consequences.
AU MacEwan, David J. (1)
CS (1) Department of Biomedical Sciences, Institute of Medical Sciences, University of Aberdeen, AB25 2ZD, Aberdeen: david.macewan@abdn.ac.uk UK
SO Cellular Signalling, (June, 2002) Vol. 14, No. 6, pp. 477-492. http://www.elsevier.com/locate/cellsig. print. ISSN: 0898-6568.
DT General Review
LA English
AB Tumour necrosis factor-alpha (TNFalpha) is a multifunctional cytokine belonging to a family of ligands with an associated family of receptor proteins. The pleiotropic actions of TNF range from proliferative responses such as cell growth and differentiation, to inflammatory effects and the mediation of immune responses, to destructive cellular outcomes such as apoptotic and necrotic ***cell*** ***death*** mechanisms. Activated ***TNF*** ***receptors*** mediate the association of distinct proteins that regulate a variety of signalling processes including kinase or phosphatase activation, lipase stimulation, and protease induction. Moreover, the cytokine regulates the activities of transcription factors, heterotrimetric or monomeric G-proteins and calcium ion homeostasis in order to orchestrate its cellular functions. This ***review*** addresses the structural basis of TNF signalling, the pathways employed with their cellular consequences, and functions. This ***review*** addresses the structural basis of TNF signalling, the pathways employed with their cellular consequences, and focuses on the specific role played by each of the two ***TNF*** ***receptor*** isotypes, TNFR1 and TNFR2.

L15 ANSWER 6 OF 134 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 2002370412 EMBASE
TI Immunobiology of tumor necrosis factor receptor superfamily.
AU Zhou T.; Mountz J.D.; Kimberly R.P.
CS T. Zhou, University of Alabama, Birmingham, AL 35294, United States. tong.zhou@ccc.uab.edu
SO Immunologic Research, (2002) 26/1-3 (323-336).
Refs: 75
ISSN: 0257-277X CODEN: IMRSEB
CY United States
DT Journal; Article
FS 005 General Pathology and Pathological Anatomy
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LA English
SL English
AB The proteins of the tumor necrosis factor (***TNF***) ***receptor*** superfamily are a group of cell-surface receptors critically involved in the maintenance of homeostasis of the immune system. By interacting with their corresponding ligands, these receptors either induce ***cell*** ***death*** or promote cell survival of immune cells. The number of recognized members of the ***TNF*** ***receptor*** and ligand superfamily has expanded substantially in the last several years. More important, the biologic function of this group of proteins has been closely associated with the regulation of the immune response and the pathogenesis of autoimmune disease. Thus, the direct targeting of these receptors by either inducing apoptosis or blocking survival of autoimmune T and B cells may be an important therapeutic strategy in the treatment of autoimmune disease. This ***review*** summarizes the recent progress in immunobiology of the ***TNF*** ***receptor*** superfamily and focuses on our studies of three critical family members - FasL/Fas, TNF-related apoptosis-inducing ligand (TRAIL)/TRAIL-Rs, and B lymphocyte stimulator (BLyS)/BLyS-Rs - to demonstrate the therapeutic potential of targeting these receptors for the treatment of autoimmune disease.

L15 ANSWER 7 OF 134 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
2
AN 2002:296624 BIOSIS
DN PREV200200296624
TI Cytotoxic signal transmission pathways via ***TNF*** family ***receptors*** .
AU Beletsky, I. P. (1); Moshnikova, A. B.; Prusakova, O. V.
CS (1) Institute of Theoretical and Experimental Biophysics, Russian Academy of Sciences, ul. Institutskaya 3, Pushchino, Moscow Region, 142290: beletsky@venus.iteb.serpukhov.su Russia
SO Biochemistry (Moscow), (March, 2002) Vol. 67, No. 3, pp. 312-328. http://www.maik.rssi.ru/cgi-bin/journal.pl?name=biochmsc&page=main. print. ISSN: 0006-2979.
DT General Review
LA English
AB Studies indicating an important role of the ***TNF*** - ***receptor*** family in control of ***cell*** ***proliferation*** , differentiation, and death have drastically increased in number in recent years. The main function of many members of this family is ***cell*** ***death*** triggering, and this is apparently the only function for some of them. Studies on the molecular mechanisms of ***cell*** ***death*** activated by members of the ***TNF*** - ***receptor*** family revealed and identified proteins directly or indirectly associated with ***TNF*** ***receptors*** . Pathways of cytotoxic signal transduction by some members of the TNF-Rs family based on currently proven protein-protein interactions and the role of distinct proteins in these processes are summarized in this ***review*** .

L15 ANSWER 8 OF 134 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 2002094271 EMBASE
TI Signaling to gene activation and ***cell*** ***death*** by tumor necrosis factor receptors and Fas.
AU Beyaert R.; Van Loo G.; Heyninck K.; Vandenabeele P.
CS R. Beyaert, Department of Molecular Biology, University of Gent-Flanders, Interuniv. Inst. for Biotechnology, B-9000 Gent, Belgium
SO International Review of Cytology, (2002) 214/- (225-272).
Refs: 343
ISSN: 0074-7696 CODEN: IRCYAJ
CY United States
DT Journal; General Review
FS 029 Clinical Biochemistry
LA English
SL English
AB Tumor necrosis factor (***TNF***) ***receptors*** and Fas elicit a wide range of biological responses, including ***cell*** ***death*** , ***cell*** ***proliferation*** , inflammation, and differentiation. The pleiotropic character of these receptors is reflected at the level of signal transduction. The cytotoxic effects of TNF and Fas result from the activation of an apoptotic/necrotic program. On the other hand, ***TNF*** ***receptors*** , and under certain conditions also Fas, exert a proinflammatory function that results from the induction of several genes. In this context, the transcription factor nuclear factor-kappa B (NF-.kappa.B) plays an important role. NF-.kappa.B is also important for the induction of several antiapoptotic genes, which explains at least partially why several cell types can only be killed by TNF in the presence of transcription or translation inhibitors. It is the balance between proapoptotic and antiapoptotic pathways that determines whether a cell will finally die or proliferate. A third signal transduction pathway that is activated in response to TNF is the mitogen-activated protein kinase cascade, which plays an important role in the modulation of transcriptional gene activation. .COPYRGT. 2002 Academic Press.

L15 ANSWER 9 OF 134 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 3
AN 2002011907 EMBASE
TI Apoptosis in the first trimester human placenta: The role in maintaining immune privilege at the maternal-foetal interface and in the trophoblast remodelling.
AU Jerzak M.; Bischof P.
CS M. Jerzak, Lab. of Reproductive Immunology, Inst. of Immunol. and Exp. Therapy, Polish Academy of Sciences, 12 R. Weigl St., 53-114 Wroclaw, Poland. jerzak@immuno.iitd.pan.wroc.pl
SO European Journal of Obstetrics Gynecology and Reproductive Biology, (10 Jan 2002) 100/2 (138-142).
Refs: 56
ISSN: 0301-2115 CODEN: EOGRAL
PUI S 0301-2115(01)00431-6
CY Ireland
DT Journal; General Review
FS 010 Obstetrics and Gynecology
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LA English
SL English
AB Apoptosis has been proposed as a mechanism for maintaining immune privilege. Expression of Fas ligand (FasL) by the human trophoblast has

been recently accepted as a mechanism providing protection against the lytic action of activated decidual immune cells expressing Fas receptor (FasR). Therefore, the purpose of this ***review*** was to determine the role of apoptosis in early pregnancy maintenance according to the latest literature. We used Medline literature search. The data suggest that apoptosis may serve as a previously unsuspected mechanism that induces tolerance of the foetal allograft against maternal immune system. Apoptosis of activated maternal immune cells occurs in the human decidua mainly through Fas-FasL or ***receptor*** for ***TNF*** -related apoptosis-inducing ligand (TRAIL-R)-TNF-related apoptosis-inducing ligand (TRAIL) signalling. This might be a defence mechanism against rejection of the foetal allograft by the maternal immune system. In addition, in this ***review*** contribution of programmed ***cell*** ***death*** to placental cell turnover and remodelling during first trimester of pregnancy is also discussed. .COPYRGT. 2002 Elsevier Science Ireland Ltd. All rights reserved.

L15 ANSWER 10 OF 134 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
DUPLICATE 4
AN 2002:269684 BIOSIS
DN PREV200200269684
TI Activation-induced ***cell*** ***death*** : The controversial role of Fas and Fas ligand in immune privilege and tumour counterattack.
AU Maher, Stephen; Toomey, Deirdre (1); Condron, Claire; Bouchier-Hayes, David
CS (1) Department of Surgery, RCSI Education and Research Centre, Beaumont Hospital, Dublin 9: toomeydeirdre@hotmail.com Ireland
SO Immunology and Cell Biology, (April, 2002) Vol. 80, No. 2, pp. 131-137. http://www.blackwell-science.com/ cgilib/jnlpage.asp?Journal=xicb&File=xicb. print.
ISSN: 0818-9641.
DT General Review
LA English
AB Activation-induced ***cell*** ***death*** (AICD) is the process by which cells undergo apoptosis in a controlled manner through the interaction of a death factor and its receptor. Programmed ***cell*** ***death*** can be induced by a number of physiological and pathological factors including Fas (CD95)-Fas ligand (FasL/CD95L) interaction, tumour necrosis factor (TNF), ceramide, and reactive oxygen species (ROS). Fas is a 48-kDa type I transmembrane protein that belongs to the ***TNF*** /nerve growth factor ***receptor*** superfamily. FasL is a 40-kDa type II transmembrane protein that belongs to the TNF superfamily. The interaction of Fas with FasL results in a series of signal transductions which initiate apoptosis. The induction of apoptosis in this manner is termed AICD. Activation-induced ***cell*** ***death*** and Fas-FasL interactions have been shown to play significant roles in immune system homeostasis. In this ***review*** the involvement of Fas and Fas ligand in ***cell*** ***death*** , with particular reference to the T cell, and the mechanism(s) by which they induce ***cell*** ***death*** is described. The role of AICD in immune system homeostasis and the controversy surrounding the role of FasL in immune privilege, inflammation, and so-called tumour counterattack is also discussed.

=> d bib abs 11-20

L17 ANSWER 11 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:557680 BIOSIS
DN PREV200100557680
TI A functional interaction between the p75 associated proteins NRIF and TRAF6.
AU Gentry, J. J. (1); Rutkoski, N. (1); Linggi, M. S. (1); Musiek, E. S. (1); Emeson, R. (1); Carter, B. D. (1)
CS (1) Biochem and Ctr Mol Neurosci, Vanderbilt Univ Med School, Nashville, TN USA
SO Society for Neuroscience Abstracts, (2001) Vol. 27, No. 2, pp. 1825. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001
ISSN: 0190-5295.
DT Conference
LA English
SL English
AB Nerve Growth Factor binding to p75 activates both a survival signal through the transcription factor ***NFkB*** , and cell death through the stress-activated kinase, JNK. NRIF, a protein shown to associate with the intracellular domain of p75, has been implicated in p75-mediated cell death, based on analysis of nrif-/- mice and the induction of apoptosis by ecotopic expression in Schwann cells. Recently, we found that NRIF interacts with TRAF6, a member of the ***TNF*** ***Receptor*** Associated Factor family, which also binds to the ICD of p75. These two p75-binding proteins could be co-immunoprecipitated when expressed in HEK cells. Interestingly, TRAF6 dramatically enhanced NRIF expression, suggesting that the interaction may stabilize NRIF protein. These proteins also functionally interacted, co-expression of NRIF increased TRAF6 activation of ***NFkB*** and JNK 2-3 fold, based on reporter assays. Moreover, when expressed alone Flag-TRAF6 or GFP-NRIF was observed throughout the cytoplasm, including some nuclear distibution of NRIF; however, when co-expressed both proteins localized exclusively in sub-nuclear domains. In contrast, TRAF6 lacking the NH2-terminus, necessary for ***NFkB*** and JNK activation, failed to translocate NRIF. This nuclear localization is particularly interesting since NRIF contains a domain homologous to a transcriptional repressor module and recombinant NRIF can bind specific DNA sequences in gel-shift assays. Taken together, these findings suggest that NRIF and TRAF6 interaction results in maximal activation of downstream signals and nuclear translocation where NRIF can bind DNA, possibly affecting cellular viability by transcriptional repression.

L17 ANSWER 12 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:186454 BIOSIS
DN PREV200200186454
TI Signaling pathway of apoptosis induced by vincristine in acute lymphoblastic leukemia cells: Activation of caspase-2 and downregulation of NF-kB are required for vincristine-induced apoptosis.
AU Zhou, Muxiang (1); Gu, Lubing (1); Findley, Harry W. (1); Woods, William G. (1)
CS (1) Pediatrics, Emory University School of Medicine, Atlanta, GA USA
SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 311a. http://www.bloodjournal.org/. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971.
DT Conference
LA English
AB The process of cancer cell death induced by certain chemotherapeutic agents is apoptosis possibly via distinct pathways, which may differ depending on various agents and different cell types. Here we report that vincristine (VCR), an important drug in chemotherapy of childhood acute lymphoblastic leukemia (ALL), induces apoptosis via a unique signaling pathway different from that induced by DNA-damaging agents, such as ionizing radiation (IR) and doxorubicin (adriamycin), as well as by TNF-alpha. Induction of p53 and activation of caspase-9 that initiate the signal transduction pathway of apoptosis induced by IR and adriamycin were not observed in VCR treated ALL cells. Instead, a specific activation of caspase-2, which executes apoptosis via death ***receptor*** such as ***TNF*** ***receptor*** , was detected in ALL cells treated with VCR. However, activation of NF-kB, which occurs in the treatment of ALL cells with TNF-alpha as well as adriamycin, was not found in ALL cells treated with VCR. In contrast, treatment with VCR significantly reduced NF-kB binding activity in an ALL cell line (EU-1) that has constitutive NF-kB activation. To further evaluate the effect of ***NFkB*** activation on chemotherapeutic agent-induced apoptosis in ALL, we transfected the dominant negative mutant inhibitor of ***NFkB*** (IkBm) into the EU-1 cells. Overexpression of IkBm significantly reduced constitutive ***NFkB*** activity in EU-1 cells, resulting in enhanced sensitivity to VCR- but not adriamycin-induced cell death examined by WST assay. Consistent with increased cell death by VCR in IkBm-transfected EU-1 cells, loss of constitutive ***NFkB*** by transfection of the super repressor significantly enhanced the activation of caspases 2 and 3 and cleavage of its substrate PARP. Therefore, our data indicate that VCR-induced apoptosis is independent of p53 and depends on activation of caspase 2 and downregulation of NF-kB, and suggests that constitutive overexpression of NF-kB in ALL cells from some patients is an important underlying mechanism of resistance to induction therapy with VCR.

L17 ANSWER 13 OF 30 CAPLUS COPYRIGHT 2002 ACS
AN 2000:270255 CAPLUS
DN 133:28857
TI Regulatory mechanisms of TRAF2-mediated signal transduction by Bcl10, a MALT lymphoma-associated protein
AU Yoneda, Takunari; Imaizumi, Kazunori; Maeda, Mitsuyo; Yui, Daishi; Manabe, Takayuki; Katayama, Taiichi; Sato, Naoya; Gomi, Fumi; Morihara, Takashi; Mori, Yasutake; Miyoshi, Ko; Hitomi, Junniti; Ugawa, Shinya; Yamada, Shuichi; Okabe, Masaru; Tohyama, Masaya
CS Department of Anatomy and Neuroscience, Osaka University Medical School, Suita, 565-0871, Japan
SO Journal of Biological Chemistry (2000), 275(15), 11114-11120
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB To elucidate the function of Bcl10, recently cloned as an apoptosis-assocd. gene mutated in MALT lymphoma, we identified its binding partner TRAF2, which mediates signaling via tumor necrosis factor receptors. In mammalian cells, low levels of Bcl10 expression promoted the binding of TRAF2 and c-IAPs. Conversely, excessive expression inhibited complex formation. Overexpressed Bcl10 reduced c-Jun N-terminal kinase activation and induced nuclear factor .kappa.B activation downstream of TRAF2. To det. whether overexpression of Bcl10 could perturb the regulation of apoptosis in vivo, we generated Bcl10 transgenic mice. In these transgenic mice, atrophy of the thymus and spleen was obsd. at postnatal stages. The morphol. changes in these tissues were caused by acceleration of apoptosis in T cells and B cells. The phenotype of Bcl10 transgenic mice was similar to that of TRAF2-deficient mice reported previously, indicating that excessive expression of Bcl10 might deplete the TRAF2 function. In contrast, in the other organs such as the brain, where Bcl10 was expressed at high levels, no apoptosis was detected. The altered sensitivities to overexpressed Bcl10 may have been due to differences in signal responses to Bcl10 among cell types. Thus, Bcl10 was suggested to play crucial roles in the modulation of apoptosis assocd. with TRAF2.

RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 14 OF 30 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 2000304002 EMBASE
TI Activation of nuclear factor .kappa.B and induction of apoptosis by tumor necrosis factor-.alpha. in the mouse uterine epithelial WEG-1 cell line.
AU Pampfer S.; Cordi S.; Cikos S.; Picry B.; Vanderheyden I.; De Hertogh R.
CS S. Pampfer, OBST 5330 Research Unit, Univ. Cath. de Louvain Med. Sch., 53 Avenue Mounier, 1200 Brussels, Belgium. pampfer@obst.ucl.ac.be
SO Biology of Reproduction, (2000) 63/3 (879-886).
Refs: 56
ISSN: 0006-3363 CODEN: BIREBV
CY United States
DT Journal; Article
FS 010 Obstetrics and Gynecology
029 Clinical Biochemistry
LA English
SL English
AB In order to better understand how tumor necrosis factor (TNF)-.alpha. may contribute to the local regulation of uterine cell death, cultures of mouse uterine epithelial WEG-1 cells were exposed to TNF-.alpha. and observed at different time intervals. Earliest decrease in cell viability was observed after 31 h of exposure to 50 ng/ml mouse TNF-.alpha. and was associated with the expression of several markers of apoptosis. Treatment with human TNF-.alpha. or addition of a neutralizing antibody against ***TNF*** -.alpha. ***receptor*** protein 80 to mouse TNF-.alpha. resulted in attenuated induction of apoptosis, suggesting that coengagement of the two ***TNF*** -.alpha. ***receptor*** types is required for maximal impact. Ceramide analogs failed to replicate the effect of TNF-.alpha. and the stress-activated protein kinase signaling pathway was not activated by the cytokine. Treatment with mouse TNF-.alpha. resulted in an increase in nuclear factor (NF)kB activity that receded after 24 h. The impact of human TNF-.alpha. on ***NFkB*** activation was more moderate. Addition of either one of three different inhibitors of ***NFkB*** (SN50, PDTC, and A771726) to mouse TNF-.alpha. sensitized WEG-1 cells to the toxicity of the cytokine. Our data suggest that WEG-1 cells initiate their response to TNF-.alpha. with an increase in ***NFkB*** activation that may have transiently biased these cells toward cell death resistance.

L17 ANSWER 15 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:418616 BIOSIS
DN PREV200000418616
TI Molecular cloning and functional characterization of murine Transmembrane Activator and CAML Interactor (TACI) with chromosomal localization in human and mouse.
AU von Bulow, Gotz-Ulrich; Russell, Helen; Copeland, Neal G.; Gilbert, Debra J.; Jenkins, Nancy A.; Bram, Richard J. (1)
CS (1) Department of Pediatrics and Adolescent Medicine, Mayo Foundation, 200 1st Street SW, Rochester, MN, 55905 USA
SO Mammalian Genome, (August, 2000) Vol. 11, No. 8, pp. 628-632. print.
ISSN: 0938-8990.
DT Article
LA English
SL English
AB The human Taci gene (Transmembrane Activator and CAML Interactor) encodes a recently discovered member of the Tumor Necrosis Factor Receptor family. TACI is expressed in B-lymphocytes and may act to regulate humoral immunity. To identify functionally important regions of the protein, we have isolated and characterized the murine homolog of the human Taci cDNA. The proteins display 61.5% similarity and 54.6% identity. Mouse TACI is a type III transmembrane protein, as judged by the lack of a cleaved signal sequence and its N-terminal extracellular exposure. The intracellular domains of the mouse and human proteins share a single, defined region of high sequence conservation (19 of 23 residues identical). This constitutes a novel domain that may play a part in the initiation of signal transduction through TACI. In support of this notion, mouse TACI was found to activate NFAT, ***NFkB*** , and AP1 transcription factors in a transient transfection assay. The Taci gene was localized to human Chromosome (Chr) 17p11 by fluorescence in situ hybridization. The murine homolog was localized by intraspecific backcross analysis to the middle of Chr 11, a region that is syntenic to human Chr 17p. This work identifies conserved domains within TACI that may mediate the cellular distribution and signal transduction function of the protein and extend the details of homology between mouse Chr 11 and human 17p.

L17 ANSWER 16 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
3
AN 2000:279667 BIOSIS
DN PREV200000279667
TI The Epstein-Barr virus latent membrane protein 1 (LMP1) enhances TNF alpha-induced apoptosis of intestine 407 epithelial cells: The role of LMP1 C-terminal activation regions 1 and 2.
AU Kawanishi, Michiko (1)
CS (1) Department of Microbiology, Graduate School of Medicine, Kyoto University, Kyoto, 606-8315 Japan
SO Virology, (May 10, 2000) Vol. 270, No. 2, pp. 258-266. print.
ISSN: 0042-6822.
DT Article
LA English
SL English
AB Epstein-Barr virus (EBV) latent membrane protein 1 (LMP1) can protect some kinds of lymphocytes from apoptotic cell death. In contrast, the present study showed that the expression of LMP1 induced high susceptibility to tumor necrosis factor alpha (TNFalpha)-induced apoptosis in intestine 407 epithelial cells, without affecting expression of ***TNF*** ***receptors*** I and II. LMP1-deletion mutants lacking either C-terminal activation region (CTAR)-1 or CTAR-2 had ability to enhance TNFalpha-induced apoptosis, whereas the deletion of both activation regions completely abolished the induction of high susceptibility to TNFalpha. Phosphorylation of the ***NFkB*** -inhibitory molecule IkB-alpha, another biological activity of TNFalpha, was not enhanced by LMP1-expression. LMP1 upregulated antiapoptotic gene A20 expression, suggesting that A20 can not block TNFalpha-induced apoptosis in this cell system. Apoptosis triggered by TNFalpha in LMP1-expressing intestine 407 cells was blocked by inhibitors of caspases-8 and -3. It is therefore concluded that in intestine 407 epithelial cells, LMP1 enhances primarily signal cascade responsible for TNFalpha-induced apoptosis, which occurs at a level upstream of acting site of caspases-8 and -3 and that CTAR-1 and CTAR-2 are involved in enhancement of TNFalpha-induced apoptosis.

L17 ANSWER 17 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:311537 BIOSIS
DN PREV200100311537
TI SDF-1 activity regulation by CD30 cross-linking in the CD4+/CD30+ cell line L540.
AU Vinante, Fabrizio (1); Rigo, Antonella (1); Pizzolo, Giovanni (1)
CS (1) Department of Clinical and Experimental Medicine, Section of Hematology, University of Verona, Verona Italy
SO Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 241a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology
. ISSN: 0006-4971.
DT Conference
LA English
SL English
AB The so far elucidated activities induced after stimulation of CD30 (a ***TNF*** -family ***receptor*** up-regulated by IL-4 and preferentially expressed/released by persistently activated Th2/0 lymphocytes) seem to integrate chemokine-driven modulation of cellular functions. Thus, we evaluated the possibility that signals transduced through CD30 may regulate some chemokines and/or chemokine receptors. To this purpose, we used the CD4+/CD30+ cell line L540, which is an established model to study CD30-mediated activation. L540 cells expressed costitutively on their membrane the SDF-1 receptor CXCR4 (MFI at flow cytometry: range 101-120; mAb from Pharmingen) and released low amounts of MIP-1 alpha (range 20-41 pg/mL) and RANTES (0.3-80 pg/mL) (Amersham ELISA kit) in standard culture conditions, while PMA stimulation induced high amounts of both chemokines. Agonistic anti-CD30 mAbs (M44 and M67, Immunex) induced nuclear mobilization of p50/p65 ***NFkB*** as well as AP-1 in supershift assays. At 48 hours, a down-regulation of membrane CD30 (p=0.008) was observed which correlated with increased sCD30 concentration in culture supernatants (mean+-SEM: basal 19.3+-5.5 vs stimulated 99.8+-12 U/mL, p=0.0006; DAKO ELISA kit). By contrast, membrane CXCR4 was up-regulated, followed by an enhancement of the chemotactic activity exerted by SDF-1 on L540 cells. This CD30-mediated effect was associated with a decrease in the rate of cell proliferation. Moreover, it was associated with no or little effect on the production of RANTES (lower than 3 pg/mL) and with an apparent inhibitory effect on the release of MIP-1 alpha (mean+-SEM: basal 33.9+-9vs stimulated 10.8+-2.3 pg/mL, p=0.026), though RPA showed a faint, early induction of MIP-1 alpha mRNA. Thus, CD30 cross-linking can lead to a modulation of CXCR4 and MIP-1 alpha expression in L540 cells modifying their sensitivity to SDF-1. This suggests that CD30-related pathways are involved in chemokine-driven activities possibly in the context of T cell priming mechanisms.

L17 ANSWER 18 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:289121 BIOSIS
DN PREV200100289121
TI Distinct signals induced by VEGF and ***TNF*** ***receptors*** converge at MEK and lead to EGR-1 and tissue factor (TF) upregulation in endothelial cells.
AU Mechtcheriakova, Diana (1); Schabbauer, Gernot (1); Lucerna, Markus (1); Binder, Bernd R. (1); Hofer, Erhard (1)
CS (1) Vascular Biology, University of Vienna, Vienna Austria
SO Blood, (November 16, 2000) Vol. 96, No. 11 Part 2, pp. 140b. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology
. ISSN: 0006-4971.
DT Conference
LA English
SL English
AB TF has been shown to be upregulated in endothelial cells not only by inflammatory cytokines such as TNF-a but also by VEGF, supporting a potential role of TFfor angiogenesis (Mechtcheriakova et al., Blood 1999; 93; 3811). Since both stimuli induce the transcription factor EGR-1, which

is critically involved in TF gene regulation, we used EGR-1 dependent TF induction as a model to identify potential cross-talk between specific signal transduction cascades initiated by VEGF and TNF. The obtained data show that VEGF mainly activates the MEK/ERK and p38 MAP kinases, whereas TNF is able to strongly activate all three major MAP kinase (MEK/ERK, p38, JNK) and the ***NFkB*** pathways. The MEK/ERK MAP kinase module appears to act as convergence point of distinct upstream VEGF and TNF-initiated signal cascades leading to TF induction via EGR-1. The VEGF signaling is characterized by a strong PKC-dependence, whereas the TNF signals can be selectively blocked by a mutant of IkB kinase-2. The involvement of PKC in VEGF signaling is a specific property of this factor, since e.g. EGF induction of MEK/ERK is independent of PKC and this is not sufficient to upregulate TF. Furthermore, it is possible that also a second factor(s) is important for the full response of the TF promoter. NFAT could be one of the candidates, since NFAT has been shown to be activated by VEGF. In line with an important role of EGR-1, the corepressor NAB2 can block VEGF-induced TF transcription. In summary, our data suggest i) a new link between the inflammatory ***NFkB*** and the MEK/ERK MAP kinase cascades, ii) a specificity of VEGF signals in comparison to other growth factors and iii) the potential use of NAB2 to inhibit VEGF/EGR-1-dependent genes.

L17 ANSWER 19 OF 30 CAPLUS COPYRIGHT 2002 ACS
AN 1999:570982 CAPLUS
DN 131:284510
TI NF-.kappa.B induces expression of the Bcl-2 homologue A1/Bfl-1 to preferentially suppress chemotherapy-induced apoptosis
AU Wang, Cun-Yu; Guttridge, Denis C.; Mayo, Marty W.; Baldwin, Albert S., Jr.
CS Laboratory of Molecular Signaling and Apoptotsis, School of Dentistry, University of North Carolina, Chapel Hill, NY, 27599, USA
SO Molecular and Cellular Biology (1999), 19(9), 5923-5929
CODEN: MCEBD4; ISSN: 0270-7306
PB American Society for Microbiology
DT Journal
LA English
AB Recent evidence indicates that the transcription factor NF-.kappa.B is a major effector of inducible antiapoptotic mechanisms. For example, it was shown that NF-.kappa.B activation suppresses the activation of caspase 8, the apical caspase in tumor necrosis factor (***TNF***) ***receptor*** family signaling cascades, through the transcriptional regulation of certain TRAF and IAP proteins. However, it was unknown whether NF-.kappa.B controls other key regulatory mechanisms in apoptosis. Here we show that NF-.kappa.B activation suppresses mitochondrial release of cytochrome c through the activation of the Bcl-2 family member A1/Bfl-1. The restoration of A1 in NF-.kappa.B null cells diminished TNF-induced apoptosis by reducing the release of proapoptotic cytochrome c from mitochondria. In addn., A1 potently inhibited etoposide-induced apoptosis by inhibiting the release of cytochrome c and by blocking caspase 3 activation. Our findings demonstrate that A1 is an important antiapoptotic gene controlled by NF-.kappa.B and establish that the prosurvival function of NF-.kappa.B can be manifested at multiple levels.
RE.CNT 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 20 OF 30 CAPLUS COPYRIGHT 2002 ACS
AN 1999:602627 CAPLUS
DN 132:31443
TI ECSIT is an evolutionarily conserved intermediate in the Toll/IL-1 signal transduction pathway
AU Kopp, Elizabeth; Medzhitov, Ruslan; Carothers, James; Xiao, Changchun; Douglas, Iris; Janeway, Charles A.; Ghosh, Sankar
CS Section of Immunobiology and Department of Molecular Biophysics and Biochemistry, Howard Hughes Medical Institute (HHMI), Yale University School of Medicine, New Haven, CT, 06520, USA
SO Genes & Development (1999), 13(16), 2059-2071
CODEN: GEDEEP; ISSN: 0890-9369
PB Cold Spring Harbor Laboratory Press
DT Journal
LA English
AB Activation of NF-.kappa.B as a consequence of signaling through the Toll and IL-1 receptors is a major element of innate immune responses. We report the identification and characterization of a novel intermediate in these signaling pathways that bridges TRAF6 to MEKK-1. This adapter protein, which we have named ECSIT (evolutionarily conserved signaling intermediate in Toll pathways), is specific for the Toll/IL-1 pathways and is a regulator of MEKK-1 processing. Expression of wild-type ECSIT accelerates processing of MEKK-1, whereas a dominant-neg. fragment of ECSIT blocks MEKK-1 processing and activation of NF-.kappa.B. These results indicate an important role for ECSIT in signaling to NF-.kappa.B and suggest that processing of MEKK-1 is required for its function in the Toll/IL-1 pathway.
RE.CNT 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d bib abs 21-30

L17 ANSWER 21 OF 30 CAPLUS COPYRIGHT 2002 ACS
AN 1999:414305 CAPLUS
DN 131:209943
TI The zinc finger protein A20 inhibits TNF-induced NF-.kappa.B-dependent gene expression by interfering with an RIP- or TRAF2-mediated transactivation signal and directly binds to a novel NF-.kappa.B-inhibiting protein ABIN
AU Heyninck, Karen; De Valck, Dirk; Vanden Berghe, Wim; Van Criekinge, Wim; Contreras, Roland; Fiers, Walter; Haegeman, Guy; Beyaert, Rudi
CS Department of Molecular Biology, Flanders Interuniversity Institute for Biotechnology, University of Ghent, Ghent, B-9000, Belg.
SO Journal of Cell Biology (1999), 145(7), 1471-1482
CODEN: JCLBA3; ISSN: 0021-9525
PB Rockefeller University Press
DT Journal
LA English
AB The zinc finger protein A20 is a tumor necrosis factor (TNF)- and interleukin 1 (IL-1)-inducible protein that neg. regulates nuclear factor-kappa B (NF-.kappa.B)-dependent gene expression. However, the mol. mechanism by which A20 exerts this effect is still unclear. We show that A20 does not inhibit TNF-induced nuclear translocation and DNA binding of NF-.kappa.B, although it completely prevents the TNF-induced activation of an NF-.kappa.B-dependent reporter gene, as well as TNF-induced IL-6 and granulocyte macrophage-colony stimulating factor gene expression. Moreover, NF-.kappa.B activation induced by overexpression of the ***TNF*** ***receptor*** -assocd. proteins ***TNF*** ***receptor*** -assocd. death domain protein (TRADD), receptor interacting protein (RIP), and ***TNF*** ***receptor*** -assocd. factor 2 (TRAF2) was also inhibited by expression of A20, whereas NF-.kappa.B activation induced by overexpression of NF-.kappa.B-inducing kinase (NIK) or the human T cell leukemia virus type 1 (HTLV-1) Tax was unaffected. These results demonstrate that A20 inhibits NF-.kappa.B-dependent gene expression by interfering with a novel TNF-induced and RIP- or TRAF2-mediated pathway that is different from the NIK-I.kappa.B kinase pathway and that is specifically involved in the transactivation of NF-.kappa.B. Via yeast two-hybrid screening, we found that A20 binds to a novel protein, ABIN, which mimics the NF-.kappa.B inhibiting effects of A20 upon overexpression, suggesting that the effect of A20 is mediated by its interaction with this NF-.kappa.B inhibiting protein, ABIN.
RE.CNT 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 22 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:46913 BIOSIS
DN PREV200000046913
TI Arsenic compounds induce apoptosis in multiple myeloma (MM): Role of ***NFKb*** -RIP pathway.
AU Pearse, R. (1); Bajenova, O. (1); Feinman, R. (1); Tang, B. (1); Childs, B. (1); Michaeli, J. (1)
CS (1) Memorial Sloan-Kettering Cancer Center, New York, NY USA
SO Blood, (Nov. 15, 1999) Vol. 94, No. 10 SUPPL. 1 PART 1, pp. 309a. Meeting Info.: Forty-first Annual Meeting of the American Society of Hematology New Orleans, Louisiana, USA December 3-7, 1999 The American Society of Hematology . ISSN: 0006-4971.
DT Conference
LA English

L17 ANSWER 23 OF 30 CAPLUS COPYRIGHT 2002 ACS
AN 2000:18895 CAPLUS
DN 132:205908
TI Induction of negative regulators of haematopoiesis in human bone marrow cells by HLA-DR cross-linking
AU Yamaguchi, Masaki; Nadler, Steve; Lee, Jong-Wook; Deeg, H. Joachim
CS Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA, 98109, USA
SO Transplant Immunology (1999), 7(3), 159-168
CODEN: TRIME2; ISSN: 0966-3274
PB Arnold, Hodder Headline
DT Journal
LA English
AB Tumor necrosis factor-alpha (TNF.alpha.) is up-regulated by crosslinking of major histocompatibility complex (MHC) class II [human leukocyte antigen (HLA)-DR] antigens on monocytes. This is done by a bacterial superantigen or anti-HLA-DR monoclonal antibody (MAb). We have previously shown that HLA-DR crosslinking results in inhibition of haematopoiesis and apoptosis. TNF.alpha. acts as a neg. regulator of haematopoiesis. Here we investigated whether HLA-DR-mediated inhibition of haematopoiesis involved TNF.alpha. and TNF.alpha.-dependent secondary signals. Anti-HLA-DR MAb H81.9 up-regulated TNF.alpha., as well as transforming growth factor .beta., interleukin (IL)-1.beta. and IL-6 in human marrow cells at the RNA (RNA) and protein level. The effect on TNF.alpha. was investigated further. Up-regulation was blocked by herbimycin A, consistent with a tyrosine kinase-dependent mechanism. Up-regulation was also blunted by the sol. ***TNF*** - ***receptor*** fusion protein TNFR:Fc, suggesting an autocrine amplification loop. Following TNF.alpha. up-regulation, there was increased expression of Fas (CD95) and Fas-ligand (Fas-L). Up-regulation of Fas and Fas-L was blocked by TNFR:Fc. Furthermore, MAb H81.9-induced apoptosis was prevented by anti-TNF.alpha. MAb and by the sol. Fas receptor, Fas-Ig, providing further evidence that the TNF effect was mediated via Fas. At the transcriptional level, crosslinking of HLA-DR by MAb H81.9 affects nuclear localization of ***NFkB*** , which is involved in the transcription of TNF.alpha.. ***NFkB*** activity is modified by changes in cellular redox potential,

and we have shown that H81.9 affects redox potential as detd. by the generation of nitric oxide. These data show that HLA-DR-initiated signals are able to trigger a cascade of neg. regulators of haematopoiesis. This model provides an opportunity to dissect signalling pathways that may be involved in the development of spontaneous marrow failure, and to devise interventions aimed at protecting haematopoiesis.
RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 24 OF 30 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 4
AN 1998397057 EMBASE
TI Nuclear factor kB-independent cytoprotective pathways originating at tumor necrosis factor receptor-associated factor 2.
AU Natoli G.; Costanzo A.; Guido F.; Moretti F.; Bernardo A.; Burgio V.L.; Agresti C.; Levrero M.
CS M. Levrero, Fondazione Andrea Cesalpino, Policlinico Umberto I, University of Rome La Sapienza, Viale del Policlinico 155, 00161 Rome, Italy. levmax@mix.it
SO Journal of Biological Chemistry, (20 Nov 1998) 273/47 (31262-31272). Refs: 69
ISSN: 0021-9258 CODEN: JBCHA3
CY United States
DT Journal; Article
FS 029 Clinical Biochemistry
LA English
SL English
AB Most normal and neoplastic cell types are resistant to tumor necrosis factor (TNF) cytotoxicity unless cotreated with protein or RNA synthesis inhibitors, such as cycloheximide and actinomycin D. Cellular resistance to ***TNF*** requires ***TNF*** ***receptor*** -associated factor 2 (TRAF2), which has been hypothesized to act mainly by mediating activation of the transcription factors nuclear factor kB (***NFkB***) and activator protein 1 (AP1). ***NFkB*** was proposed to switch on transcription of yet unidentified anti-apoptotic genes. To test the possible existence of ***NFkB*** -independent cytoprotective pathways, we systematically compared selective trans-dominant inhibitors of the ***NFkB*** pathway with inhibitors of TRAF2 signaling for their effect on TNF cytotoxicity. Blockade of TRAF2 function(s) by signaling-deficient oligomerization partners or by molecules affecting TRAF2 recruitment to the ***TNF*** ***receptor*** 1 complex completely abrogated the cytoprotective response. Conversely, sensitization to TNF cytotoxicity induced by a selective ***NFkB*** blockade affected only a fraction of TNF-treated cells in an apparently stochastic manner. No cytoprotective role for c-Jun amino-terminal kinases/stress-activated protein kinases (JNKs/SAPKs), which are activated by TRAF2 and contribute to stimulation of activator protein 1 activity, could be demonstrated in the cellular systems tested. Although required for cytoprotection, TRAF2 is not sufficient to protect cells from TNF + cycloheximide cytotoxicity when overexpressed in transfected cells, thus indicating an essential role of additional ***TNF*** ***receptor*** 1 complex components in the cytoprotective response. Our results indicate that TNF-induced cytoprotection is a complex function requiring the integration of multiple signal transduction pathways.

L17 ANSWER 25 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1998:228293 BIOSIS
DN PREV199800228293
TI hUBC9 associates with MEKK1 and type I ***TNF*** -alpha ***receptor*** and stimulates NFkappaB activity.
AU Saltzman, Alan; Searfoss, George; Marcireau, Christophe; Stone, Maureen; Ressner, Rose; Munro, Robin; Franks, Carol; D'Alonzo, Jill; Tocque, Bruno; Jaye, Michael; Ivashchenko, Yuri (1)
CS (1) Rhone-Poulenc River Central Res., Gene Med. Dep., 500 Arcola Rd., Collegeville, PA 19426 USA
SO FEBS Letters, (April 3, 1998) Vol. 425, No. 3, pp. 431-435. ISSN: 0014-5793.
DT Article
LA English
AB hUBC9, an E2 ubiquitin conjugating enzyme, was identified by yeast two-hybrid screening and coprecipitation studies to interact with MEKK1 and the type I ***TNF*** -alpha ***receptor*** , respectively. Because both of these proteins regulate ***NFKB*** activity, the role of hUBC9 in modulating NFkappaB activity was investigated. Overexpression of hUBC9 in HeLa cells stimulated the activity of NFkappaB as determined by NFkappaB reporter and IL-6 secretion assays. hUBC9 also synergized with MEKK1 to activate NFkappaB reporter activity. Thus, hUBC9 modulates NFkappaB activity which, at least in part, can be attributed to its interaction with MEKK1 and the type I ***TNF*** -alpha ***receptor*** .

L17 ANSWER 26 OF 30 CAPLUS COPYRIGHT 2002 ACS
AN 1997:740095 CAPLUS
DN 127:355669
TI Method of enhancing the effect of neurotrophin with analogs of p75NTR367-379
IN Riopelle, Richard J.; Weaver, Donald F.; Ross, Gregory M.; Shamovsky, Igor L.
PA Shamovsky, Igor L., Can.; Queen's University At Kingston; Riopelle, Richard J.; Weaver, Donald F.; Ross, Gregory M.
SO PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9740809	A2	19971106	WO 1997-CA271	19970423
WO 9740809	A3	19980326		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2252469	AA	19971106	CA 1997-2252469	19970423
AU 9725634	A1	19971119	AU 1997-25634	19970423
US 6417159	B1	20020709	US 1997-839131	19970423

PRAI GB 1996-8335 A 19960423
WO 1997-CA271 W 19970423
AB The present invention provides methods and compns. for enhancing an effect or effects of a neurotrophin, preferably, but not limited to, enhancing the growth and survival promoting properties of neurotrophins. The cytoplasmic region of the common neurotrophin receptor (p75NTR) (rat, human, chick) contains a putative membrane-assocg. domain implicated in intracellular signaling. A peptide (R3) identical to this domain (p75NTR367-379) and various analogs of this peptide displayed CD spectra in aq. and non-polar environments identical to the amphiphilic tetradecapeptide mastoparan (MP), and were internalized by PC12 rat pheochromocytoma cells. The R3 peptide enhanced neurite growth in PC12 cells, chick embryo primary sensory neurons, and fetal rat primary sensory neurons in vitro in the presence of sub-satg. concns. of NGF. Peptide analogs of R3 not faithful to the distance and angular relationships of ionic groups, and the putative amphiphilic structure of p75NTR367-379, while still providing some enhancement, nevertheless displayed reduced potency to enhance NGF-mediated neurite growth. The common neurotrophin receptor p75NTR activates and translocates the nuclear transcription factor ***NFkB*** and displays pro-apoptotic effects similar to other members of the ***TNF*** ***receptor*** superfamily. A peptide mimic of the amphiphilic domain 367-379 of p75NTR that enhances TrkA mediated neurite growth by NGF, was used to affinity purify cytoplasmic proteins from PC12 cells. Isolated proteins contained a predominant species with an apparent mol. wt. of 65 kDa. The affinity purified 65 kDa protein, as well as a protein of similar mol. mass from crude cell exts., were identified by immunoblotting with antibody to NF.kappa.B. The 65 kDa species was chem. cross-linked to the radiolabeled analog of the peptide mimic of p75NTR and immunopptd. by antibody to ***NFkB*** . These observations, taken together with the finding that a p75NTR-selective NGF antagonist blocked mediated neurite growth in limiting NGF conditions, support the view that p75NTR participates in neurite growth via a signaling pathway involving the translocation of NF.kappa.B.

L17 ANSWER 27 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1996:123955 BIOSIS
DN PREV199698696090
TI Apoptosis mediated by the ***TNF*** -related cytokine and ***receptor*** families.
AU Ware, Carl F. (1); Vanarsdale, Sammee; Vanarsdale, Todd L.
CS (1) Div. Biomedical Sci., Univ. California, Riverside, CA 92521 USA
SO Journal of Cellular Biochemistry, (1996) Vol. 60, No. 1, pp. 47-55. ISSN: 0730-2312.
DT General Review
LA English
AB T lymphocytes use several specialized mechanisms to induce apoptotic cell death. The tumor necrosis factor (TNF)-related family of membrane-anchored and secreted ligands represent a major mechanism regulating cell death and cell survival. These ligands also coordinate differentiation of tissue to defend against intracellular pathogens and regulate development of lymphoid tissue. Cellular responses are initiated by a corresponding family of specific receptors that includes two distinct TNFR (TNFR60 and TNFR80), Fas (CD95), CD40, p75NTF, and the recently identified lymphotoxin beta-receptor (LT-beta-R), among others. The MHC-encoded cytokines, TNF and LT-alpha, form homomeric trimers, whereas LT-beta assembles into heterotrimers with LT-alpha, creating multimeric ligands with distinct receptor specificities. The signal transduction cascade is initiated by transmembrane aggregation (clustering) of receptor cytoplasmic domains induced by binding to their multivalent ligands. The TRAF family of Zn RING/finger proteins bind to TNFR80; CD40 and LT-beta-R are involved in induction ***NFKB*** and cell survival. TNFR60 and Fas interact with several distinct cytosolic proteins sharing the "death domain" homology region. TNF binding to TNFR60 activates a serine protein kinase activity and phosphoproteins are recruited to the receptor forming a multicomponent signaling complex. Thus, TNFRs use diverse sets of signaling molecules to initiate and regulate cell death and survival pathways.

L17 ANSWER 28 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 5
AN 1994:449642 BIOSIS
DN PREV199497462642
TI Acid sphingomyelinase is not essential for the IL-1 and tumor necrosis

factor receptor signaling pathway leading to ***NFkB*** activation.
AU Kuno, Kouji; Sukegawa, Kazuko; Ishikawa, Yuji; Orii, Tadao; Matsushima, Kouji (1)
CS (1) Dep. Pharmacol., Cancer Res. Inst., Kanazawa Univ., Takara-Machi 13-1, Kanazawa 920 Japan
SO International Immunology, (1994) Vol. 6, No. 8, pp. 1269-1272. ISSN: 0953-8178.
DT Article
LA English
AB A recent report has suggested that tumor necrosis factor (TNF) utilizes acid sphingomyelinase (SMase) pathway to activate ***NFkB*** (Schulze et al. 1992. Cell 71:765). To directly investigate the role of acid SMase in IL-1 and ***TNF*** ***receptor*** -mediated signal transduction, we examined the ability of Niemann-Pick disease (NPD) type A fibroblasts, which are deficient in acid SMase, to induce IL-8 gene expression through activating ***NFkB*** . Unexpectedly, IL-1-alpha and TNF-alpha efficiently induced IL-8 production and IL-8 mRNA in NPD type A fibroblasts as in normal fibroblasts. Furthermore, activation of ***NFkB*** was also induced in NPD type A fibroblasts in response to IL-1-alpha and TNF-alpha stimulation to a similar extent as in normal fibroblasts. These results provide evidence that acid SMase is not essential in IL-1 and ***TNF*** ***receptor*** signaling leading to ***NFkB*** activation as well as the cytokine gene activation which is regulated by ***NFkB*** .

L17 ANSWER 29 OF 30 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 92156130 EMBASE
DN 1992156130
TI Mechanisms of tumor necrosis factor action.
AU Schutze S.; Machleidt T.; Kronke M.
CS Inst. fur Med. Mikrobiologie/Hygiene, Technische Universitat Munchen, Trogerstr. 4a,8000 Munchen 80, Germany
SO Seminars in Oncology, (1992) 19/2 SUPPL. 4 (16-24). ISSN: 0093-7754 CODEN: SOLGAV
CY United States
DT Journal; Conference Article
FS 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LA English
SL English
AB Tumor necrosis factor (TNF) is able to induce a great diversity of cellular responses via modulating the expression of a number of different genes. The multitude of TNF activities may be explained by both structural and functional heterogeneity in ***TNF*** ***receptors*** as well as by a diversification of postreceptor signal transduction pathways. Purification of ***TNF*** ***receptors*** has revealed two major, distinct binding proteins (TR60 and TR80). TR60 seems to be an essential component for TNF signaling; the functional role of TR80 remains to be elucidated. The pathway of postreceptor signal transduction involves phospholipase A2, a phosphatidylcholine-specific phospholipase C, protein kinase C, and other serine/threonine and tyrosine-specific protein kinases with as yet unknown function. At the receiving end of TNF signaling, induction of gene expression is mediated through activation of nuclear transcription factors, such as ***NFkB*** , AP-1, IRF-1, and NF-GMa.

L17 ANSWER 30 OF 30 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1991:38574 BIOSIS
DN BR40:15554
TI TNF INDUCED ***NFKB*** -HIV-1-LTR ACTIVATION CAN BE EFFICIENTLY BLOCKED
BY AN ANTI- ***TNF*** - ***RECEPTOR*** P60 ANTIBODY.
AU KRUPPA G; MEICHLE A; THOMA B; SCHEURICH P; PFIZENMAIER K; KROENKE M
CS CLINICAL RES. GROUP, MAX-PLANCK SOCIETY, GOSSLERSTR. 10D, 3400 GOETTINGEN, FRG.
SO SEVENTH INTERNATIONAL LYMPHOKINE WORKSHOP, SAN ANTONIO, TEXAS, USA, OCTOBER 1-5, 1990. LYMPHOKINE RES. (1990) 9 (4), 573. CODEN: LYREDH. ISSN: 0277-6766.
DT Conference
FS BR; OLD
LA English

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	ENTRY	SESSION	
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